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REPEATED LUMBAR PUNCTURES OF SPINAL DRAINAGE

DIAGNOSTIC AND THERAPEUTIC VALUE IN TRAUMATIC AND ALLIED LESIONS OF THE CENTRAL NERVOUS SYSTEM

WILLIAM SHARPE, M.D.
NEW YORK

The use of lumbar puncture as an important aid in the diagnosis of lesions of the central nervous system has become much more frequent within the past ten years; no longer is the test considered an "operation," deferred until the increasing severity of the patient's condition demands an accurate diagnosis and then often used as a last resort. Even today, however, in many hospitals lumbar puncture is employed only for diagnostic purposes and only in selected conditions, but the use of repeated lumbar punctures of spinal drainage in acute traumatic intracranial lesions is considered dangerous and radical!

During the past twenty years in this clinic, the use of diagnostic lumbar punctures has become progressively more frequent and earlier, as a part of the routine examination of any patient having complaints severe enough to warrant reference to a neurologic clinic.[1] As a diagnostic aid, there has been little or no criticism of its possible danger, except in subtentorial expanding lesions, and even in these conditions, if the lumbar puncture is properly performed, there is no danger of a serious complication: diagnostic lumbar punctures, and by all means therapeutic lumbar punctures, should always be performed with the manometric attachment, preferably the mercurial one; in this manner, the pressure of the cerebrospinal fluid can be accurately registered, and under no circumstances should an amount of cerebrospinal fluid be withdrawn to lower the pressure more than one half of the initial pressure. For diagnostic purposes alone, 2 cc. of fluid is amply sufficient, but for therapeutic purposes, it is at times possible to withdraw slowly 20 cc. and even more before the pressure is lowered to one half of the initial pressure. In these therapeutic cases, however, the free escape of the cerebrospinal fluid from the puncture needle, when no manometer is being used to estimate the pressure until the pressure is lowered to a point far below one half of the initial pressure, is attended by the well known definite danger of medullary complications of direct pressure by the foramen magnum collar, as well as intracranial vascular alterations to the degree of spontaneous rupture of the arterioles themselves. Such lumbar punctures, especially without the use of the manometer, are not properly performed and therefore the possible resulting complications are not valid criticisms of the test itself. In this clinic in a period of twenty years, serious complications following lumbar punctures have occurred in only three patients, and in each case the test itself had not been properly performed—the cerebrospinal fluid having been allowed to escape freely from the needle without the manometric attachment and, therefore, no pressure reading having been made. In each of these earlier cases, necropsy disclosed that the rapid lowering of the high intracranial pressure had forced the median portion of the cerebellum into the foramen magnum. In no other patients have complications occurred during or following the lumbar puncture properly performed with the aid of the mercurial manometer.

The observations in this paper will be limited, first, to acute traumatic intracranial lesions in adults, children and the new-born; secondly, to acute traumatic lesions of the spinal cord, and, in the third place, to acute spontaneous intracranial hemorrhage of the subarachnoid type, so often diagnosed and confused clinically as cases of "apoplexy" within the internal capsule. Repeated lumbar punctures of spinal drainage to lessen the symptoms in selected conditions of diffuse purulent meningitis will merely be mentioned.

ACUTE TRAUMATIC INTRACRANIAL LESIONS

1. *In Adults.*—As is now commonly recognized, the important factor in acute cases is not a fracture of the skull, whether of the vault or of the base, but an increased intracranial pressure, whether due to hemorrhage or to acute cerebral edema and increased amount of cerebrospinal fluid or to both. The presence of a fracture merely demonstrates that the cranial injury was sufficient to fracture the skull, and naturally fractures of the base are the more serious as indicative of a greater force at the time of the cranial impact in order to produce an indirect fracture, and, therefore, the much greater danger of associated complications of intracranial hemorrhage and acute cerebral edema. The presence of the fracture is frequently also of value in permitting free blood and excess cerebrospinal fluid to escape from the cranial cavity; a natural decompression and drainage thus results in lowering any marked intracranial pressure. However, in acute cases of cranial injury, if the intracranial pressure is markedly increased, this important fact should be determined as soon as possible after the patient has survived the period of initial shock.

The only accurate method of determining the presence of an increased intracranial pressure is by the

Read before the Section on Nervous and Mental Diseases at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 15, 1934.

1. Sharpe, William: Diagnosis and Treatment of Brain Injuries With and Without a Fracture of the Skull, Philadelphia, J. B. Lippincott Company, 1920.

lumbar puncture. However, no prolonged examinations such as roentgenograms and lumbar puncture tests should be made until the patient has recovered from the initial shock of the injury, as such examinations merely prolong the shock. If the patient cannot recover from the shock with all the treatment directed to that end, surely neurologic examinations and tests will not lessen the shock, and they may even increase it.

If the diagnostic lumbar puncture reveals clear fluid under a normal pressure (from 6 to 8 mm. of mercury), or if the pressure is only slightly increased to 10 mm. and at the most to 12 mm., or if the fluid is merely blood tinged, a favorable prognosis may be given, the general condition of the patient being good and in the absence of serious internal bodily injuries. On the other hand, if the pressure of the cerebrospinal fluid is markedly increased to more than twice the normal (from 14 to 16 mm.) and especially if it is bloody, the diagnostic lumbar puncture should be converted into a therapeutic one of spinal drainage by withdrawing slowly an amount of fluid to lower the pressure to one half of the initial pressure recorded. That is, if the initial pressure reads 20 mm., then only an amount of fluid should be withdrawn to lower the pressure to 10 mm. and not below 10 mm. In this manner, there is no danger of medullary complications or of increasing intracranial hemorrhage. The latter fear, so often expressed in the literature, that lumbar punctures theoretically will permit greater intracranial hemorrhage to occur has not been observed in this clinic when a lumbar puncture has been properly performed with the aid of the manometer as previously described.

By use of the test tube rack, whereby the cerebrospinal fluid withdrawn at each puncture of spinal drainage is placed in a test tube and labeled consecutively with the date and the exact time attached, as the blood settles at the bottom of the tubes, the blood percentage can be estimated approximately and the lessening blood percentage of successive punctures is clearly demonstrated. Specimens may also be centrifugated or sent to the laboratory for accurate red blood cell counts, but in this clinic the tube rack is considered a most impressive demonstration for the entire staff to observe the therapeutic value of repeated lumbar punctures of spinal drainage. Depending on the height of the increased intracranial pressure and the degree of percentage of blood in the cerebrospinal fluid, the frequency of the repeated lumbar punctures of spinal drainage will vary from one to two or three daily, and, in severe cases showing both high pressure and high blood percentage of the cerebrospinal fluid as many as four spinal drainage punctures each day (one every six hours) have given the best results. In these borderline cases, which are comparatively rare, if the high pressure and the blood percentage of the cerebrospinal fluid are not progressively lowered by the consecutive lumbar punctures, early cranial operation and drainage are indicated, before the patient reaches the serious period of medullary compression. To permit the intracranial hemorrhage to form a layer of supracortical clot during the period of expectant palliative treatment merely lessens the chances for a good end-result if the patient recovers and also makes operative cranial decompression and drainage imperative in the more severe cases.

In this clinic diagnostic lumbar punctures are part of the routine neurologic examination on all patients having acute head injuries of a severity warranting their being brought to the hospital. Occasionally, the results of this test are surprising in cases of apparently trivial head injuries, which would be clinically diagnosed as simple concussion, contusions or laceration of the scalp without the aid of lumbar puncture. In this manner, cases of slowly increasing extradural hemorrhage have been immediately suspected by a definite rise of the pressure of clear cerebrospinal fluid, even in the absence of positive roentgenograms, and an early differential diagnosis of an increasing extradural hemorrhage from acute cerebral edema and excess cerebrospinal fluid is greatly aided by the amount of fluid withdrawn in order to lower the pressure to one half of the initial pressure recorded.

In the treatment of acute head injuries when the diagnostic lumbar puncture discloses clear or merely blood tinged cerebrospinal fluid under normal or only slightly increased pressure, the routine expectant palliative method, aided by dehydration of varying degrees, is usually entirely satisfactory and the end-results are excellent. In these cases, even without lumbar punctures, the end-results would be the same, but the physician can never be certain in regard to the intracranial status without the diagnostic lumbar puncture. Also, if during the convalescence, symptoms and signs of an intracranial complication develop, then the results of this initial lumbar puncture will be of the greatest value for a comparison with those of a later test in order to determine accurately the progress of the intracranial condition. Only too frequently patients having apparently minor head injuries become gradually or suddenly worse during the first week; if the diagnostic lumbar puncture in the initial period has been negative, any marked rise of pressure, whether due to hemorrhage or to excess cerebrospinal fluid or to both, can be easily determined and treated accordingly.

In cases in which the initial diagnostic lumbar puncture discloses hemorrhage of a mild degree, or a moderately increased pressure of cerebral edema and an excess amount of cerebrospinal fluid, the patient will receive naturally more careful attention, especially dehydration will be added to the expectant palliative treatment, and the physician will be constantly on the lookout for the development of symptoms and signs of an increasing intracranial pressure. If these symptoms and signs appear, another lumbar puncture should be performed immediately to determine accurately the intracranial status.

In cases in which the initial lumbar puncture reveals a cerebrospinal fluid pressure of over 12 mm., whether or not the fluid is bloody in the experience of this clinic the expectant palliative treatment, aided by dehydration and the repeated lumbar punctures of spinal drainage, is eminently satisfactory in the vast majority of patients; so much so that the advisability of cranial operations of decompression and drainage has been greatly lessened. At the time of my last report on this subject in 1928,[2] the operative treatment of acute brain injuries was advised in 31 per cent of the cases, but now, up to Jan. 1, 1934, this figure has been lowered to 26 per cent, the decrease in operative treatment being due chiefly to the more persistent use of repeated lumbar punctures of spinal drainage. Dehydration is of temporary value only in the less seriously injured patients having a moderate degree of cerebral edema and an excess of cerebrospinal fluid, especially in the absence of much blood in the cerebrospinal fluid.

2. Sharpe, William: Neurosurgery; Principles, Diagnosis and Treatment, Philadelphia, J. B. Lippincott Company, 1928.

Patients in whom the cerebrospinal fluid has a blood percentage higher than 10 should not be dehydrated for fear of hastening the coagulation of the free blood before it can be absorbed or drained, and thus a layer of supracortical hemorrhagic clot of varying amount may be formed. There is a real danger that the organized residue of the blood clot may later produce cortical instability and even a partial blockage of the absorption of the cerebrospinal fluid. This causes a chronic condition of the "wet" brain type, associated with persistent headaches, vertigo, early fatigue and changes of personality of the depressed or irritable type, and even convulsive seizures.

During the past twenty years in this clinic the total mortality of traumatic cranial lesions has been greatly lowered so that now it is less than 29 per cent, and with the exclusion of those patients who are admitted to the hospital in a moribund condition and die within six hours from shock and internal injuries, the mortality is 18 per cent. Naturally, in the alcoholic, arteriosclerotic and nephritic type of patient, the prognosis must always be grave, since even apparently trivial bumps on the head may produce a severe degree of cerebral edema and the rapid development of a terminal medullary edema.

2. *In Children.*—Fortunately, acute traumatic cerebral edema and an excess amount of cerebrospinal fluid are comparatively rare occurrences in children. There is also lessened danger of hemorrhage following head injuries, but any child with a cranial trauma of severity warranting admission to the hospital should, in my opinion, receive the careful examination suggested for adults and should be treated accordingly. In children under 12 years of age, the expectant palliative treatment, aided by dehydration in selected cases, and repeated lumbar punctures of spinal drainage, has been entirely satisfactory in 78 per cent, and in only 14 per cent has it been considered advisable to institute cranial drainage, in order to save the life and furnish the best possible chance for the ultimate recovery of function and normality. So often in the past, the end-results in patients having head injuries have been overlooked. The immediate saving of life is important, yet surely the efforts of the physician should be directed to include physical and especially mental recoveries, which are almost equally important socially.

3. *In the New-Born.* — A tremendous advance has been made within recent years in the diagnosis and treatment of acute cerebral birth hemorrhage. The diagnosis is now no longer deferred for months after birth in order to await the appearance of signs of an intracranial lesions with delayed physical and mental development, such as inability to hold up the head, inability to sit up, increasing spasticity of the arms or legs and delayed speech. It is the present practice to perform diagnostic lumbar puncture immediately in a new-born baby, whether or not it was born by an instrumental labor, if there is difficulty in nursing, refusal to nurse or abnormal stupor, especially in the presence of twitchings of the extremities or of the facial muscles, or even, in rare cases, convulsive seizures. If free blood is present in the cerebrospinal fluid, repeated lumbar punctures of spinal drainage are immediately instituted, just as in adults and children with head injuries, in order to permit the free blood to escape and thus avoid the great danger, not only of death but in some cases the even more tragic result of spasticity and retarded mentality. If the diagnostic lumbar puncture reveals clear cerebrospinal fluid, the physician knows almost certainly that no intracranial hemorrhage has occurred and that the signs were most probably due to a temporary cerebral edema of varying degree.

In cases in which the cerebrospinal fluid is bloody, all treatment, and not including the injection of mother's blood and other coagulants, should be directed toward aiding the natural absorption of the blood by draining as much of it as possible, and thus lessen its blood percentage, before it can coagulate to form the organization-residue of unabsorbed supracortical hemorrhage—the direct cause of future physical and mental cerebral signs. Once this fibrous organization residue has been formed about the supracortical veins in the sulci, there results the serious probability of a partial blockage in the absorption of the normal cerebrospinal fluid through the stomas of exit in the walls of these supracortical veins, and thus is presented the great danger of a chronic "wet" brain of the external hydrocephalic type, associated with an increased intracranial pressure of varying degree. It is this later development of increased intracranial pressure, and not a primary damage to the brain at the time of the acute hemorrhage at birth, that produces the chronic spastic paralysis and mental retardation in these patients. In a percentage of only one in sixteen cases in a large series has there been any pathologic evidence of a primary brain injury.

In acute cases of cerebral birth hemorrhage, the early diagnostic lumbar puncture disclosing bloody cerebrospinal fluid under varying degrees of increased pressure is converted into a therapeutic spinal drainage; owing to the presence of the open cranial fontanels, there is apparently no danger of producing medullary compression by permitting as much of the bloody cerebrospinal fluid to escape as will do so. In this clinic, these therapeutic lumbar punctures are repeated every two hours until the blood percentage of the cerebrospinal fluid becomes less than 10, and then every six to twelve hours until the fluid is practically clear. The average number of spinal drainage punctures has been five in the milder cases, and as many as twelve in the more serious ones with extensive hemorrhage under high intracranial pressure.

This method of spinal drainage has been eminently successful in over 80 per cent of the cases of acute cerebral birth hemorrhage, and in no case in this clinic has it been necessary to advise a cranial drainage of the hemorrhage during the past four years. This is also due to the fact that in the cases of massive gross hemorrhage, such as follow rupture of the tentorium with cerebral and cerebellar laceration, the child is in a severe condition of shock and is usually moribund, so that no cranial operation nor even spinal drainage can be considered. It is, however, the milder cases that are so frequently overlooked, in which the signs are often vague and indefinite; these cases should have the benefit of an early diagnostic lumbar puncture, and if bloody cerebrospinal fluid is revealed, the repeated lumbar punctures of spinal drainage should be instituted immediately in the hope that all the hemorrhage can be drained, the great danger of later physical and mental impairment being thus avoided. In many of these acute cases the patients are now apparently normal in every respect as the result of the outlined treatments, whereas, once the condition has been permitted to become chronic, the most that can be expected from any known treatment is an improvement, never normality.

ACUTE TRAUMATIC LESIONS OF THE SPINAL CORD

As in cranial injuries, the important factor in trauma of the spinal column is not the presence of fracture of the bony structure but rather the degree of involvement of nerve tissue; naturally, depressed fractures of the skull should be elevated soon after recovery from the initial shock. Likewise, direct bony compression of the spinal cord resulting from vertebral fracture dislocation should be relieved early; the one and only exception being the patient having such a marked fracture dislocation of the vertebrae that the spinal cord must have been irreparably and completely damaged by severance or extreme compression and therefore presenting a hopeless prognosis. Any operative procedure advised in these tragic cases merely discredits the operation and the surgeon.

Fortunately, however, the cases of direct bony compression of the spinal cord itself are comparatively rare —and the much more common condition in conjunction with fracture dislocation is the presence of partial or complete spinal canal block, whether due to a narrowing of the bony canal from the associated fracture dislocation, or, as frequently happens, to an edematous enlargement of the cord itself, to a degree that the canal may be entirely blocked at the site of the trauma. Just as in cranial injuries, the swollen edematous brain, together with hemorrhage and excess cerebrospinal fluid, may produce an increased intracranial pressure sufficient to cause medullary compression and even death of the patient, so in traumatic lesions of the spinal cord the swollen edematous cord with varying degrees of subarachnoid hemorrhage may so fill and block the canal that a direct compression of the cord itself results in the clinical picture of acute transverse myelitis. Unless this extreme blockage is relieved at the earliest possible moment, many cord fibers may be considered permanently and hopelessly damaged.

An early diagnostic lumbar puncture to permit the use of the Queckenstedt test in order to determine the presence of canal block is absolutely essential in the rational treatment of patients having cord lesions. If no canal block is present, only the routine expectant palliative treatment with the usual orthopedic measures of immobilization and traction is indicated. If, however, a partial block of the canal is demonstrated by the Queckenstedt test, then, just as in traumatic intracranial lesions associated with increased pressure of hemorrhage, cerebral edema or excess cerebrospinal fluid, the diagnostic lumbar puncture is converted into a therapeutic one of spinal drainage, and as much bloody cerebrospinal fluid is drained as possible in the hope that the canal blockage can be lessened. In almost one half of our cases of partial canal block, in the absence of marked fracture dislocation to the degree of a definite kyphosis, spinal drainage of repeated lumbar punctures together with the usual measures of dehydration was sufficient to lessen and even remove the block; and when lumbar drainage failed, combined lumbar and cisternal punctures were entirely satisfactory. In no case of partial canal block in the absence of marked bony displacement was a spinal decompression of laminectomy necessary.

In cases of complete canal block, unless the vertebral fracture dislocation is so extensive that no amount of spinal and cisternal drainage could relieve the cord compression, the patients should be given the opportunity of having the canal block lessened by combined lumbar-cisternal drainage of repeated punctures; if no immediate lessening of the canal block is demonstrated, an early laminectomy of direct spinal decompression and drainage should be performed to give the patient the greatest possible chance of improvement. The longer the delay, the greater the irreparable damage to nerve tissues by the continued compression. If the neurologist cannot state with certainty that the entire cord in cases of clinically acute traumatic transverse myelitis is irreparably damaged—and one cannot except when the roentgenograms reveal a vertebral malalinement of such a degree that the cord must have been destroyed—the patient, in my opinion, should have the possible benefit of lumbar and cisternal drainage, and if that fails to lessen the canal block, then the advisability of an immediate decompression laminectomy should be considered. Patients having the clinical picture of complete transverse myelitis should not be condemned to a hopeless future without at least a determination of whether there is a canal block. Months later they may begin to move the toes, then the legs, and in rare cases they may even stand. Such partial improvement is not uncommon and clearly demonstrates the fact that the diagnosis of complete acute traumatic transverse myelitis cannot be made with certainty, because some of the cord fibers may not be irreparably damaged, and unless the canal block of vertebral malalinement is so extreme that the entire cord must have been destroyed, every opportunity should be given to the patient to obtain the greatest possible recovery of function.

ACUTE SPONTANEOUS INTRACRANIAL HEMORRHAGE OF THE SO-CALLED APOPLEXY SUBARACHNOID TYPE IN THE ELDERLY

Careful histories and thorough physical and neurologic examinations are always most important and essential in the diagnosis and treatment of these patients, and, as an additional aid, the diagnostic lumbar puncture is of real value. It is not dangerous when properly performed in the manner described, for determining a definite diagnosis in the spontaneous cerebral accidents and vascular encephalopathies of the elderly. The latter vague generalizations of nomenclature are no longer satisfactory and only rarely is it impossible to classify with accuracy the character, as well as the localization and extent of the vascular lesion.

A diagnostic lumbar puncture that reveals clear cerebrospinal fluid is naturally not repeated, and not more than from 1 to 2 cc. of cerebrospinal fluid is removed for laboratory examination. Clear cerebrospinal fluid immediately eliminates subarachnoid and ventricular hemorrhage, so that the lesion, if hemorrhagic, is localized most probably in the internal capsule or infrequently within the cerebral hemispheres. In the latter cases an increased intracranial pressure of varying degree is disclosed. In these cases of clear cerebrospinal fluid the possibilities also include arterial blockage of a thrombotic or embolic character, or simply a transient arteriospasm.

If, on the contrary, the cerebrospinal fluid at lumbar puncture is bloody, any form of arterial blockage is immediately excluded, and the diagnosis becomes limited to subarachnoid hemorrhage or to an extensive internal capsular hemorrhage that has ruptured into the ventricle, producing the most serious type of apoplexy, or to a massive cerebral hemorrhage that has ruptured into the subarachnoid spaces or into either lateral ventricle. Naturally, the history of the patient, including

the preexisting symptoms and signs, the character of the onset of the acute illness, the examination of the heart, the blood pressure, the urinalysis and, of the greatest importance, a painstaking neurologic examination, in addition to the results of the lumbar puncture, will make possible the accurate diagnosis and localization of the lesion in almost all these cases of cerebral accidents.

With a diagnosis of subarachnoid hemorrhage, it has been the experience in this clinic that repeated lumbar punctures of spinal drainage not only permit a more rapid recovery of physical, mental and emotional functions of the patient but the degree of improvement may be so increased that the ultimate functional recovery may approximate normality.

During the past three years, nineteen patients have been admitted to the hospital with the final diagnosis of spontaneous subarachnoid hemorrhage of the elderly, and, without a diagnostic lumbar puncture, in seven of these patients the diagnosis would have been impossible. Just as in cases of cranial injuries, the diagnostic lumbar puncture should never be performed before the patient has recovered from the initial shock.

In patients having bloody cerebrospinal fluid when the diagnostic lumbar puncture is made, the pressure of the fluid was registered by the mercurial manometer and only enough bloody cerebrospinal fluid was removed to lower the pressure to one half of the initial pressure. Depending on the height of the increased pressure and on the degree of blood percentage in the cerebrospinal fluid, repeated lumbar punctures of spinal drainage were performed once a day in the milder cases and as many as six times a day in the more severe cases of extensive subarachnoid hemorrhage. Five therapeutic lumbar punctures have been done in the average case, the largest number in any one patient being eleven before the cerebrospinal fluid became straw colored and under normal pressure (from 6 to 8 mm. of mercury). In no patient in this series of cases of simple subarachnoid hemorrhage has the condition become worse following the diagnostic lumbar puncture, and in each case the blood percentage has lessened in the successive therapeutic punctures of spinal drainage. In no patient in this series of cases of bloody cerebrospinal fluid has cranial drainage been considered either necessary or advisable; if spinal drainage is successful in eventually clearing the cerebrospinal fluid of blood, naturally cranial drainage is not indicated.

In the severe cases either of extensive internal capsular hemorrhage or of massive cerebral hemorrhage rupturing into the ventricles, the clinical picture was frequently one of profound shock at first, followed by the rapid onset of bilateral spasticity with rising temperature, so that not even a diagnostic lumbar puncture was to be considered; the mortality has been 100 per cent in these moribund patients. Fortunately, these most serious types of massive spontaneous hemorrhage are comparatively rare, as are the complete thromboses that have occurred in this clinic, the much more common types of so-called apoplexy being the subarachnoid as described, with an excellent prognosis, and also the frequent cases of arteriospasm of only temporary impairment. The much described internal capsular hemorrhage of varying degree, and usually limited to a small area of the capsule itself, must not be confused with the described lesions, and usually a careful neurologic examination makes the differentiation possible. This is also true of the internal capsular thromboses of embolic origin.

SELECTED CASES OF DIFFUSE PURULENT MENINGITIS

As a last resort, repeated lumbar and cisternal punctures of spinal drainage may be used as a symptomatic treatment to relieve the persistent severe headache of high intracranial pressure. They may prove of real value, and occasionally the patient may recover with life. Such patients might have recovered without spinal drainage, and yet if the headaches are lessened and the patient's general condition is improved and no ill effects of spinal drainage are demonstrable, surely the advisability of this expectant palliative method of treatment should at least be considered. Naturally, the lumbar punctures should be properly performed, as in hemorrhagic intracranial lesions. The spinal mercurial manometer should always be used to estimate the initial pressure and only the amount of cerebrospinal fluid necessary to reduce the pressure one half and not lower than one half should be permitted to escape. If the spinal puncture is done in this manner there will be no danger of any medullary complication of foramen magnum compression or other unfavorable signs.

CONCLUSIONS

1. Lumbar puncture is an important diagnostic aid, and repeated lumbar punctures of spinal drainage are of therapeutic value in selected cases of traumatic and allied lesions of the central nervous system.

2. Diagnostic and therapeutic lumbar punctures are without danger when properly performed. The manometric attachment should always be used and only the amount of cerebrospinal fluid necessary to lower the pressure to one half of the initial pressure should be withdrawn.

3. In the most frequent subarachnoid type of traumatic intracranial and spinal hemorrhage, in adults, children and the new-born, and in the spontaneous subarachnoid "apoplexies" of the elderly, repeated lumbar punctures of spinal drainage not only reduced the mortality but give a higher percentage of recovery of function.

4. Therapeutic lumbar punctures of spinal drainage, combined with dehydration, have lessened by about 20 per cent the advisability of operative cranial drainage in head injuries in adults and by more than 50 per cent in the new-born.

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ABSTRACT OF DISCUSSION

DR. TEMPLE FAY, Philadelphia: In 1921 I introduced the method of "dehydration" as a therapeutic means of treating these acute traumatic cases. This year I had the opportunity of reviewing cases of head trauma covering a period of fourteen years. In this series about half of the cases were treated by the older methods. Therapeutic and diagnostic lumbar puncture was not done and surgical decompression was frequently resorted to. The mortality was 26 per cent. Following the advent of spinal drainage and dehydration, the mortality dropped so that in the latter half of the series it has never exceeded 18.2 per cent. This includes all patients that entered the hospital whether they lived three minutes or three weeks. After the third hour the mortality dropped sharply to 14 per cent, where spinal drainage and dehydration were employed, and this mortality has been a consistent one over a period of ten years. I believe it can be said that there is ample clinical evidence in favor of the conservative methods described. Lumbar puncture should be undertaken with a full knowledge of the mechanisms involved so as to avoid the dangers Dr. Sharpe has described. It is perfectly obvious that if the ventricular system is "open" and one reduces the fluid pressure so that there is an equalization of the loss of fluid from within

the brain ventricles and from without simultaneously, no actual mass movement of the brain in the direction of the foramen magnum will occur. If, however, lumbar puncture is not done until after the first day and the symptoms then require lumbar puncture, there may be real danger because of a tremendous mass edema of the brain with no free fluid spaces open, owing to a diffuse interstitial edema with cellular swelling. I believe that delayed lumbar puncture affords a very distinct danger of foraminal hernia. If one is going to adopt the method, it should be adopted sincerely from the very beginning: either no lumbar puncture following the old school of thought, or frequent drainage as the best means of restoring oxygen and nutrition to the brain throughout a period of compression so that it may survive. Spinal drainage and reduction of intracranial pressure, after all, simply mean providing the additional space required by cerebral circulation during the period of swollen brain cells, hemorrhage, or an overaccumulation of spinal fluid. Spinal drainage, properly performed, has undoubtedly proved to be a valuable adjunct to treatment.

DR. A. S. CRAWFORD, Detroit: Dr. Sharpe is one of the pioneers whose teachings and writings have stimulated the much wider use of lumbar puncture as a diagnostic and therapeutic means in treating these cases. As Dr. Fay has said, this has led to a clearer understanding of the conditions and has resulted, in a way, in greater conservatism, because it has helped to cure many cases without operation. In a careful analysis of more than 1,300 cases of definite craniocerebral injuries in the last eleven years, I found that during the last three years there has gradually been a tendency toward more conservatism in the use of lumbar puncture. At one time it was being done in nearly 50 per cent of the cases and now I find it necessary for diagnostic or therapeutic purposes in something over 10 per cent. Mortality rates have gradually become lower. I do not know that these two factors are necessarily interrelated, but I do know that as experience increases I am able to carry more cases through the critical period without the use of lumbar puncture. On the other hand, I feel that if there is any question of the diagnosis or prognosis a lumbar puncture should be done. If it is done carefully, as pointed out by the speaker, with fine needles and withdrawing slowly, there is very little risk. Of course, it must be realized that there is a great deal of risk in a certain type of case in which there is gross blood and blockage of the posterior fossa. With regard to treatment of hemorrhage in children, I have been able, by means of punctures, and particularly when I have found the localized blood, to save some in whom spastic paraplegias would have developed. I remember two cases in which I put a needle in the cisterna and found gross blood. I was able to remove that blood and then go a little farther in and find clear spinal fluid, showing that the hemorrhage was subdural but extra-arachnoid. These patients were going down hill rapidly and probably would have died, had the obstruction not been relieved. They were entirely cured. I think this is a subject which should be brought up periodically, because the reporting of experiences adds to the fund of knowledge and permits the application of better judgment.

DR. NED R. SMITH, Tulsa, Okla.: I wish to present a thought from the standpoint of the consulting neurologist who lives in a community in which there is no neurosurgeon. The traumatic head cases are for the most part seen by the general surgeon, and occasionally the neurologist is called in consultation. A month ago I heard a paper by an eminent neurosurgeon who deprecated the use of the lumbar puncture. At the end of that paper, I was convinced that he was quite sound in his point of view. At the end of Dr. Sharpe's paper, I am convinced that in his hands the lumbar puncture method and drainage has certain phases of distinct value. It seems to me that the weight of evidence thus far would point to the judicious use of the well known method of dehydration by intravenous and other types of medication, plus the always available diagnostic method of lumbar puncture if necessary.

DR. PAUL C. BUCY, Chicago: I have always been a little perplexed by this difficulty about lumbar puncture or no lumbar puncture. The general surgeon has never outlined a standard method of treating all abdominal injuries. He doesn't set up a group of rules and say "We will always do this" and "We will never do that." His treatment of the abdominal injury depends on what the intra-abdominal condition is. If the bladder is ruptured, he treats it one way; if the liver or spleen is ruptured, he treats it another way. In other words, he individualizes the treatment for the type of injury. The same thing is true of cranial injuries to a large extent. They are not all alike, in spite of the fact that they are classed more or less together under cranial or cerebral injury. What is needed is individualization of treatment and adaptation of treatment to the needs of the case. It seems to me just as illogical to say that we will always do a lumbar puncture as it is to say we will never do a lumbar puncture. I think that if our cases are studied and the necessary treatment applied in accordance with what exists in a given patient, the end results will be distinctly better. As to operation on head injuries, my experience with the subject is not as extensive as Dr. Sharpe's or Dr. Fay's. Nevertheless, if one excludes the cases of depressed fracture and intracranial hemorrhage, I have yet to see the patient who needs an operation, a decompression, if you like.

DR. S. D. SWOPE, El Paso, Texas: The neurologist, the psychiatrist and the neurosurgeon must go hand in hand in work of this character. Few of us are able to combine those three qualities. They are so distinct and so characteristic in their requirements that one man can hardly complete all of them in the course of a lifetime. The diagnostic value of a lumbar puncture is always dependent on the careful examination of the patient from all sources. In the clinic with which I am affiliated, practically every psychiatric case is carefully examined by lumbar puncture. The prevalence of syphilitic infection alone would require that procedure in a community where the disease is probably more prevalent than in any other section of the United States. I would call attention to the importance of early decision in cases of birth injury. The average psychiatrist does not see the effect of birth injury until it is too late to accomplish anything in the way of specific results. The fact is that a baby born today and crying for the next three days in all probability has a cerebral injury, and that cerebral injury can be benefited only by immediate attention. The importance of lumbar puncture certainly depends on the amount of pressure, and all our lumbar punctures are regulated by mercury manometers, which will give us the nearest we can get to a natural result. I thoroughly concur in the suggestion that as a general rule the removal of 50 per cent of the pressure is amply sufficient, but there are times when conditions exist in which the removal must extend much further, and that also is a matter of judgment, which, after all, is the best armamentarium the physician has.

DR. A. L. SKOOG, Kansas City, Mo.: I agree with the author regarding the dangers, but if it is in the hands of a man who has had adequate experience, who has mechanical skill and a good knowledge of the central nervous system, the dangers may be reduced to nil, particularly if he selects his cases after careful neurologic examination. Regarding the type of manometer, I see no reason why one can't use either a mercury or a water manometer. Possibly in some cases the water manometer may be better.

DR. ADRIAN VERBRUGGHEN, Chicago: It is possible to divide skull fractures into certain categories and to suggest appropriate treatment for each category. First there is the type of patient who comes into the hospital with a head injury and is in severe shock and obviously about to die. I doubt whether it is wise to intervene in a case of this type except to treat the shock. Certainly one would not attempt to do a lumbar puncture in this type of case merely to find out whether the fluid is blood or not. There is a second type of patient who is admitted with a head injury, who may be slightly irrational but is relatively conscious and who will in all probability get better if he is left alone, and I cannot see any reason for not leaving him alone. There is another type of patient who is received into the hospital unconscious and whose level of consciousness and whose neurologic signs remain the same. One feels in these cases that anything which can be done to turn the tide in their favor should be done and for that reason an attempt is made to reduce the increased intracranial pressure. It seems that in these cases lumbar puncture, with halving of

the spinal manometric pressure, offers one of the principal indications of puncture. This, combined with the repeated intravenous injections of hypertonic dextrose solution, may be sufficient to turn the balance in favor of the patient. There is still another type of patient who does not require lumbar puncture—the patient who is draining cerebrospinal fluid from his ear or nose. He is performing a continuous lumbar puncture on himself. I must agree entirely with Dr. Bucy's unfavorable attitude toward decompression in head injury and certainly experience at the Cook County Hospital of Chicago confirms this. At this hospital decompression is very rarely performed for the purpose of relieving intracranial pressure. However, if an individual goes on for forty-eight hours or more in an unconscious state in spite of lumbar puncture and dehydration, it has been thought wise to perform decompression in some of these cases in order to afford an additional means of reducing the intracranial pressure.

DR. WILLIAM SHARPE, New York: There is no treatment that can be standardized. In the Pan-American Clinic we look on diagnostic puncture as simply a test, just as one would test the reflexes or have roentgenograms taken, or any of the other tests in neurology. It is not a dangerous procedure in our experience, and I defy any neurologist to tell with any degree of certainty what the intracranial status is in these acute head injuries unless a lumbar puncture is performed. Many cases presenting merely contused scalps and no neurologic signs whatever have shown a blood percentage above 50 and it may be possible in some cases for the natural means of absorption to take care of all that blood so that no residue is left and the patient can regain his normality. I am thinking of normality in addition to recovery of life, and I think that in the past the profession has considered the patient who has been able to leave the hospital rather than the end result as to the normality of a patient able to earn his living and hold his job. I had that experience in looking over the records of four of the leading hospitals in New York over a ten-year period, ten years after their discharge. Of the patients I could find, and I found about 30 per cent of them, 34 per cent plus were having symptoms and signs of their head injury. It was ascertained that in those patients still having symptoms and signs years after the head injury, frequently in the notes in the hospital I found "persistent headache, dizzy spells and increased blood pressure," which often was raised 10 or 15 points, and of course in that period, twenty years ago, no lumbar puncture had ever been performed. It was the period when the ophthalmoscopic examination of the fundi was considered sufficient to determine an increased intracranial pressure in a traumatic lesion. Dr. Fay asked whether in dehydrating patients with bloody cerebrospinal fluid there would be any organic evidence later that possibly the dehydration did have some effect on the early coagulation of the free blood in the cerebrospinal fluid. I have been called to see patients when dehydration had been used and when there had been very bloody cerebrospinal fluid, and if operation was indicated on the fourth, fifth or sixth day the blood was found to be coagulated. Usually in these cases the blood does not coagulate for seven, eight or ten days ordinarily, so that it seemed to me that the dehydration did hasten the coagulation of the free blood and, naturally, that is something one wishes to avoid for fear of a clot formation. The early accurate diagnosis by lumbar puncture in all of these cases is therefore important. I agree with Dr. Bucy in regard to operations for head injuries.

The Two Laws of Euclid.—Thus while modern physical science makes headlines for itself so fast there is difficulty even for experts to keep up with it, Sir James Jeans publicly acknowledges that photons, electrons and protons, though their properties can be expressed mathematically, are really as meaningless as x, y and z to a child on its first lesson in algebra; and it has been admitted by someone else that the advance of physical knowledge is at present reduced to the extraction of one incomprehensible from another incomprehensible. Yet we are assured that the mathematical starting point for all this was Hero's synthesis of the two laws of Euclid which have merely been expanded by Newton, Einstein and Sulaiman to embrace all the activities of the universe.—Cushing, Harvey: The Humanizing of Science, *Science* **81**:137 (Feb. 8) 1935.

STUDIES ON THE THYROTROPIC HORMONE OF THE ANTERIOR PITUITARY

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A study of the physiologic activity of the thyrotropic hormone of the anterior pituitary has shown that the stimulating effect of the hormone on the thyroid gland is only temporary and that retrogressive changes actually take place in spite of continued injections of the hormone. Korenchevsky [1] injected rats with a glycerol extract of the anterior pituitary for periods of from six to eleven weeks. A decrease in the weight of the thyroid gland was found, which averaged 17 per cent below the control weight. Siebert and Smith [2] and Verzar and Wahl [3] noted that the rise in metabolic rate of guinea-pigs injected with thyrotropic hormone reached a peak by the tenth day and then returned to the normal level. The latter showed that a marked drop in basal metabolic rate occurred when the hormone was injected into thyroidectomized guinea-pigs. Houssay,

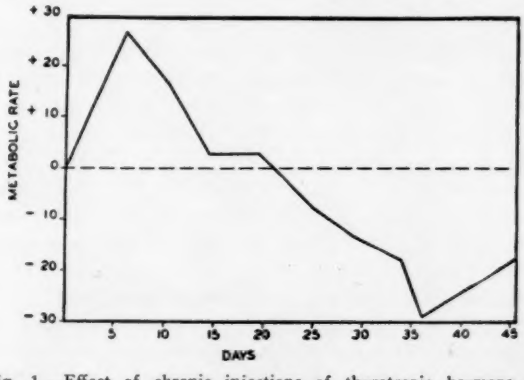

Fig. 1.—Effect of chronic injections of thyrotropic hormone on the metabolism of normal rats (average of eleven animals).

Biasotti and Mazzocco [4] have reported that anterior pituitary extract causes a fall in the blood iodine of thyroidectomized dogs, which is the opposite of the response to the thyrotropic hormone in normal and hypophysectomized animals. Lee and Gagnon [5] found that anterior pituitary extract caused a lowering of the metabolic rate of rats when injected for a prolonged period, the metabolic levels in some instances going as low as from 10 to 39 per cent below the preinjection value. Evans and Sarka [6] obtained basal metabolic rates 18 per cent below the preinjection value in rats chronically treated with anterior pituitary extracts. Retrogressive changes in the thyroid gland of guinea-pigs and ducks treated over a long period with anterior

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pituitary extracts have been noted by Aron,[7] Loeb and Friedman,[8] Schockaert,[9] Thurston [10] and Friedgood.[11]

We have followed the changes in metabolic rate of a group of rats injected with large doses of a purified extract of thyrotropic hormone (fig. 1). A rise in the metabolic rate occurs during the first week of injections, reaching a peak of plus 28 per cent; the metabolism then drops to the preinjection value by the second or

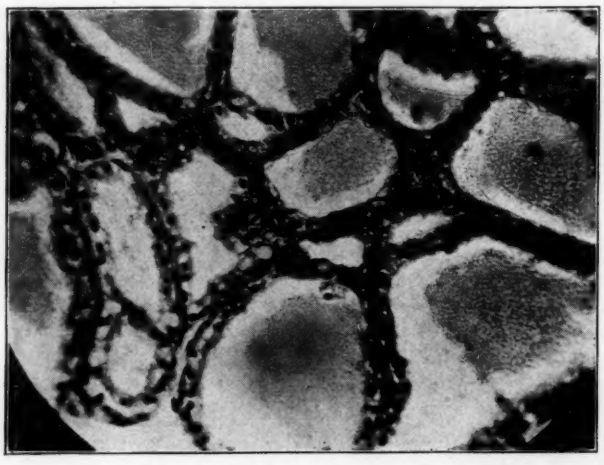

Fig. 2.—Normal thyroid gland of rat.

third week and continues to fall, going as low as minus 29 per cent by the fifth week. This is the level of metabolism of the untreated hypophysectomized rat.[12] The microscopic appearance of the thyroid at this stage of treatment resembles that of the untreated hypophysectomized animal (figs. 2 and 3). The pituitary glands of the animals injected with thyrotropic hormone for a long period of time give a negative response when tested for the presence of thyrotropic hormone, although they still contain the growth hormone.[13]

In studying the nature of this apparent resistance to the thyrotropic hormone, we have found that the serum of animals which have been injected for a long period of time with thyrotropic hormone contains a substance that is capable of inhibiting the action of thyrotropic hormone. The serum from these rats, when given in doses of from 0.5 to 1 cc. twice daily for three days to hypophysectomized rats, prevented a rise in metabolic rate with amounts of thyrotropic hormone equal to 200 times the minimum effective dose (fig. 4). A similar finding was obtained when normal rats and guinea-pigs were used as test animals.[14]

We have injected a horse with thyrotropic hormone for a period of four months. After one month the antithyrotropic substance was found to be present in the horse's serum. Extracts of the antithyrotropic serum of the horse have been prepared which, when given in doses of 0.4 cc., are capable of inhibiting the action of 100 units of thyrotropic hormone in the normal rat (fig. 5). Larger amounts of the extract, up to 4 cc. daily, not only inhibit the action of 100 units of thyrotropic hormone injected into normal rats but at the same time apparently inhibit the thyrotropic hormone of the animal's own pituitary gland, causing a fall in metabolic rate to minus 24 per cent, which is the metabolic rate of the hypophysectomized animal.

The antithyrotropic substance appears to be unstable. Boiling the extract at p_H 5 for three minutes completely destroys the inhibitory substance. Furthermore, the extract has been found to lose a considerable degree of its potency when kept in sterile ampules in the refrigerator for two months. When kept at room temperature the potency was entirely lost after this time.

We have obtained the inhibitory substance in the serum of animals of different species that have been injected with thyrotropic hormone. In addition to the rat and horse, the guinea-pig, rabbit and dog have been studied. We have tested the blood from a small group of patients that have been given therapeutic injections of thyrotropic hormone, and we have evidence of the presence of the inhibitory substance in the serum of such cases. This finding is doubtless the explanation for the numerous negative reports on the clinical use of thyrotropic hormone. We have evidence also of the antithyrotropic hormone occurring spontaneously in the serum of certain patients exhibiting low basal metabolic rates.

The mechanism of the action of the antithyrotropic substance is not understood. It does not inhibit the action of thyroxine. Rats injected with thyrotropic hormone for periods of from forty to seventy days showed practically the same response to a given amount of thyroxine as normal animals. Furthermore, the giving of antithyrotropic serum in conjunction with thyroxine did not prevent a rise in metabolism. This would suggest that we are dealing with a substance quite different from diiodotyrosine, which Abelin [15] has found to antagonize thyroxine, and also "Katechin" of Blum,[16] which has the same property. Abelin and Wegelin [17] showed that simultaneous injections of diiodotyrosine with anterior lobe preparations prevent the marked hyperplasia of the thyroid that is seen with

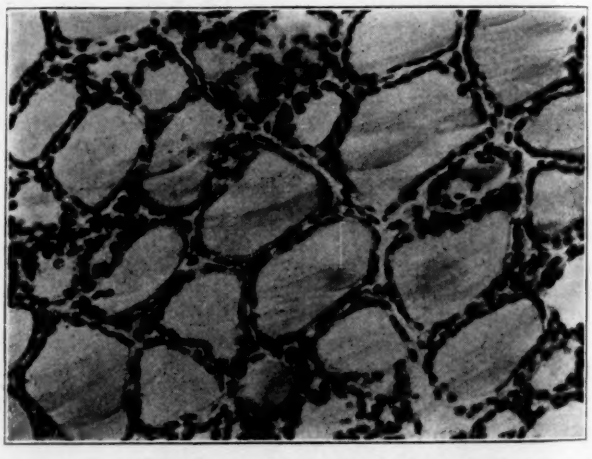

Fig. 3.—Involutional atrophy of thyroid after injection of thyrotropic hormone for two months. This resembles the thyroid of the hypophysectomized rat.

the latter alone. Anselmino and Hoffmann [18] have prepared a lipoid soluble extract of normal blood which also inhibits the action of thyroxine. Herold [19] has shown that this lipoid extract of normal blood prevents

7. Aron, M.: Compt. rend. Soc. de biol. **103**: 145 (Jan. 24) 1930.
8. Loeb, Leo, and Friedman, H.: Proc. Soc. Exper. Biol. & Med. **29**: 172 (Nov.) 1931.
9. Schockaert, J. A.: Am. J. Anat. **49**: 379 (Jan.) 1932.
10. Thurston, E. W.: A Comparison of Hypertrophic Changes in Thyroid, Arch. Path. **15**: 67 (Jan.) 1933.
11. Friedgood, H. B.: Bull. Johns Hopkins Hosp. **54**: 48 (Jan.) 1934.
12. Anderson, Evelyn M., and Collip, J. B.: J. Physiol. **82**: 11 (Aug. 24) 1934.
13. Anderson, E. M., and Collip, J. B.: Lancet **1**: 784 (April 14) 1934.
14. Collip, J. B., and Anderson, Evelyn M.: Lancet **1**: 76 (Jan. 13) 1934.
15. Abelin, I.: Biochem. Ztschr. **233**: 483, 1931.
16. Blum, F.: Schweiz. med. Wchnschr. **63**: 777 (Aug. 12) 1933.
17. Abelin, I., and Wegelin, C.: Klin. Wchnschr. **11**: 2103 (Dec. 17) 1932.
18. Anselmino, K. J., and Hoffmann, F.: Klin. Wchnschr. **12**: 99 (Jan. 21) 1933.
19. Herold, L.: Ztschr. f. exper. Med. **90**: 684, 1933.

hyperplasia of the thyroid in rats treated with small doses of thyrotropic hormone but that extract of blood from pregnancy and exophthalmic goiter [20] had no such action.

It is to be hoped that a study of the combined action of the thyrotropic and antithyrotropic hormones on the thyroid gland may clear up some of the discrepancies between changes in function of the thyroid

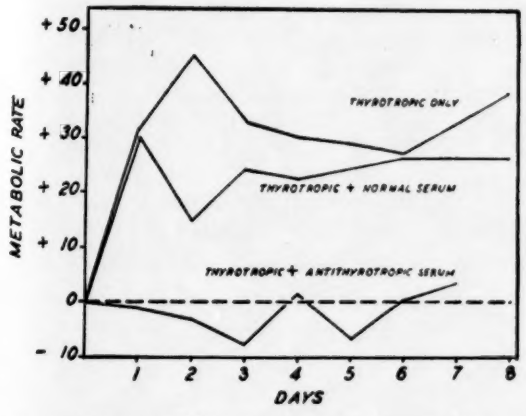

Fig. 4.—Complete inhibition of thyrotropic hormone by the antithyrotropic serum tested on hypophysectomized rats.

gland and the cellular activity. As is stated earlier in this paper, when the animal has built up its own antithyrotropic substance as a result of prolonged injections of thyrotropic hormone the thyroid gland undergoes hyperinvolution until it resembles somewhat the atrophic thyroid seen in the hypophysectomized animal. On the other hand, in an attempt to find the amount of antithyrotropic hormone which would just inhibit the action of a definite amount of thyrotropic hormone, we have found that a given amount of antithyrotropic hormone may be sufficient to prevent the rise in metabolic rate without inhibiting the production of hyperplasia of the thyroid by the thyrotropic hormone. Hypophysectomized rats that received both thyrotropic and antithyrotropic hormones for from seven to ten days showed hyperplastic changes at the end of this period,

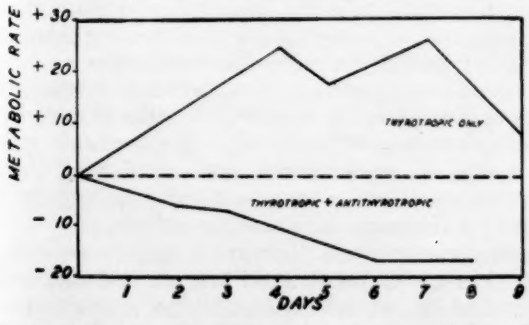

Fig. 5.—Effect of antithyrotropic extract on the metabolism of normal rats treated with thyrotropic hormone.

associated with a lowered metabolic rate, which was depressed in some instances to 38 per cent below normal (fig. 6). It has been shown by a number of workers [21] that the injection of thyrotropic hormone causes an outpouring of organic iodine from the thyroid gland. This is coincident with the appearance of vacuoles in the colloid of the gland and a rise in the metabolic rate of the animal. These changes have been noted twenty-four hours after the first injection of the hormone. Hyperplastic changes in the thyroid appear later. One might possibly interpret the cellular changes in the thyroid as a compensatory effect in an attempt to replenish thyroid secretion that is being released from the gland. This would be in keeping with Marine's [22] view that hyperplasia of the thyroid is due to a functional insufficiency of the gland.

In a large series of rats and guinea-pigs in which we have studied the morphologic changes of the thyroid coincident with changes in metabolic rate during treatment with thyrotropic hormone, we have found it difficult in many cases to correlate the microscopic appearance with the physiologic changes, as indicated by the metabolic rate. On the sixth day of injections of thyrotropic hormone in the rat one usually finds an increase in metabolic rate of 28 per cent and hyperplastic changes in the thyroid gland. On the tenth day of treatment the metabolic rate has dropped to plus 10 per cent; hyperplasia of the thyroid is still present, although evidence of involutionary changes may be seen (fig. 7). Scattered throughout the gland are large

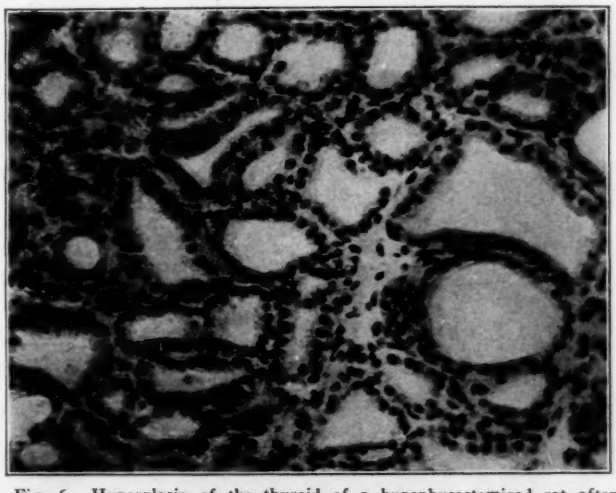

Fig. 6.—Hyperplasia of the thyroid of a hypophysectomized rat after seven daily injections of thyrotropic and antithyrotropic hormones. The metabolic rate was minus 26 per cent.

vesicles lined with a very flat epithelium and distended with a deeply staining colloid. By the fourteenth day of treatment a residual hyperplasia may still be present, but one usually finds the follicles lined with a flat epithelium and filled with dense colloid (fig. 8); the metabolic rate at this time has returned to the normal level. However, one frequently finds exceptional cases; for instance, one animal with a metabolic rate of plus 41 per cent on the fourteenth day of injection showed marked involutional atrophy of the thyroid; in another case the metabolic rate had dropped to minus 18 per cent by the fourteenth day, while hyperplasia was still seen in the gland. Oehme, Paal and Kleine [23] have reported a similar observation in which there was present a very active thyroid following injections of thyrotropic hormone without an increase in metabolism.

A group of goitrous rats in which the thyroid morphology resembled the hyperplasia seen in exophthalmic goiter showed a subnormal metabolism; in some cases the rates were as low as minus 17 per cent. A severe

20. Herold, L.: Klin. Wchnschr. **13**: 1242 (Sept. 1) 1934.
21. Schockaert, J. A., and Foster, G. L.: J. Biol. Chem. **95**: 89 (Feb.) 1932. Closs, K.; Loeb, L., and MacKay, E. M., ibid. **96**: 585 (June) 1932. Loeser, A.: Arch. f. exper. Path. u. Pharmakol. **163**: 530, 1931. Grab, W., ibid **168**: 715, 1932.
22. Marine, David: Report of the International Goiter Conference, Bern, Hans Huber, 1927.
23. Oehme, C.; Paal, H., and Kleine, H. O.: Arch. f. exper. Path. u. Pharmakol. **171**: 1, 1933.

hyperthyroidism developed in these animals when thyrotropic hormone was given; the metabolic rates varied from plus 120 to plus 200 per cent. The animals that died, death being due apparently to thyrotoxicosis, showed beginning involutional atrophy of the thyroid.

Evidence has been gathered in the study of the physiologic properties of the thyrotropic hormone which suggests that the anterior pituitary may play an etiologic rôle in exophthalmic goiter. The finding of an antithyrotropic hormone brings in another factor that needs to be correlated with the present knowledge of thyroid disease. The injection of thyrotropic hormone produces a condition of hyperthyroidism in normal animals, which is only temporary because of the occurrence of large amounts of an inhibitory substance that antagonizes the action of the thyrotropic hormone. In exophthalmic goiter there is the condition that has been described as a "thyroid diarrhea," which causes the thyroid gland to pour out excessive amounts of thyroid hormone. Presumably the hyperplasia of the gland is an attempt to compensate for the rapid loss of its hormone. The characteristic course of the disease is a cyclic variation of acute exacerbations and remissions of hyperthyroid symptoms. The occurrence of an infection frequently is associated with a relapse of hyperthyroidism. Changes in the physiology of other endocrine organs, as in pregnancy, often coincide with a return of the hyperthyroidism. If one may assume that in the normal individual there is a balance between the thyrotropic hormone of the anterior pituitary and the inhibitory substance, one may then expect an upset of the balance to occur in clinical hyperthyroidism, which is characterized either by an increase in the thyrotropic hormone or by a decrease in the inhibitory substance. An increase of the thyrotropic hormone probably occurs in those cases of acromegaly in which there is evidence of increased activity of the thyroid gland. In exophthalmic goiter in which no evidence of any objective changes in the anterior pituitary gland is found, the mechanism for the production of the antithyrotropic substance may possibly be defective. We have found that bacterial toxins increase the sensitivity of the experimental animal to thyrotropic hormone. It might be assumed that the toxin has interfered with the production of the inhibitory substance. One must consider also in the condition of the nontoxic parenchymatous goiter whether an upset in the balancing mechanism is present, with either a decrease of the thyrotropic hormone or an increase of the antithyrotropic substance. It is likely that a great many factors influence the balance of this mechanism of the stimulator and inhibitor and that there are also intrinsic factors in the thyroid gland which are responsible for the disturbance in its physiology.

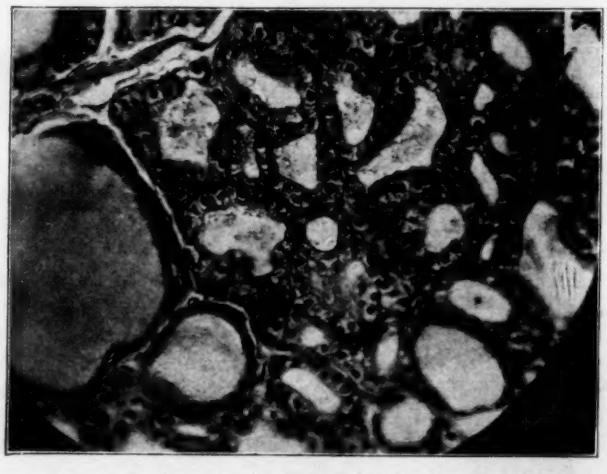

Fig. 7.—Hyperplasia of thyroid of rat with beginning involution.

One of us has postulated recently the theory of the principle of inverse response and of antihormones. Briefly stated, these theories are as follows: 1. The responsiveness of an individual to administered hormone varies inversely with the hormone content or production of the subject's own gland. 2. For each hormone there is an opposite, an antagonistic or antihormone substance. 3. The absolute amount of a hormone and of its respective antagonist determines the degree of stability of the subject so far as this one particular endocrine function is concerned. The hormone antihormone complex may be regarded as a buffer system. Some individuals of a species may appear on superficial study to be normal as regards some endocrine function, yet they may have a decrease or an increase in the respective hormone buffer system, and this condition may be detected only when abnormal responses are obtained following the administration of hormone extracts. As has been mentioned previously, it follows that a supposedly hyperhormone state may in actuality be due not to an increase in the production of a specific hormone but to a decrease in the corresponding antagonistic substance. Also the converse condition—namely, a supposedly hypohormone state—may be due to an increased amount of antihormone. Endocrine dysfunction in general may be regarded as primarily a hormone antihormone imbalance.

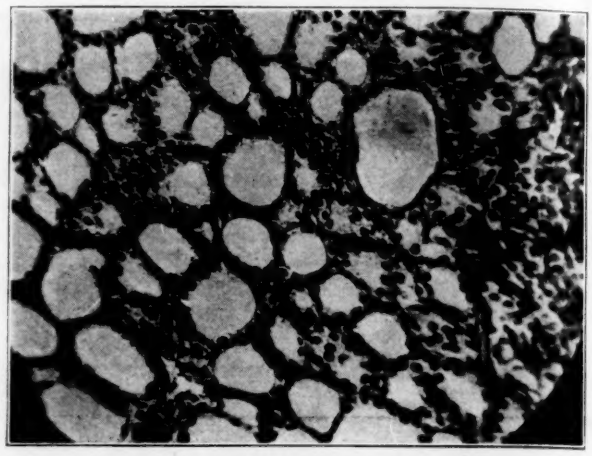

Fig. 8.—Involution of the thyroid of the rat after fourteen daily injections of thyrotropic hormone.

These theories were enunciated largely on account of the clear-cut demonstration that we had obtained of the production, in readily detectable amounts in the serum of animals treated with thyrotropic hormone, of a substance that was antagonistic to the thyrotropic hormone. More recently, there have been made in our laboratory a number of observations that tend to support the theory as stated. Thus we have evidence of the existence of an antiketogenic substance,[24] of an antigrowth substance, of an antimaturity factor (pituitary) and of an antigonadotropic substance.[25] The active prin-

24. Black, P. T.; Collip, J. B., and Thomson, D. L.: J. Physiol. **82**: 385 (Aug. 17) 1934.

25. Selye, Hans; Collip, J. B., and Thomson, D. L.: Proc. Soc. Exper. Biol. & Med. **31**: 487 (Jan.), 566 (Feb.), 1934. Selye, Hans; Bachman, C.; Thomson, D. L., and Collip, J. B., ibid. **31**: 1113 (June) 1934. Bachman, C.; Collip, J. B., and Selye, Hans, ibid. **32**: 544 (Dec.) 1934.

ciple in an antiserum produced as a result of long continued daily injections of hormone extracts may be regarded quite rightly as a possible antibody reaction to the administered extract (antigen). We prefer to think, however, of the antagonistic principles present in the serum of chronically treated animals as normal constituents of blood, the level of which has been increased by the treatment. We are encouraged further in this belief since we have found in the serum of certain human patients antithyrotropic substance and in other human cases an antimaturity substance. These patients had not been treated, but there had occurred in them spontaneously a hormone imbalance resulting in the predominance of the respective antisubstance. Also we have been able to antagonize the estrogenic effect and in part the ovarian effect of a maturity hormone extract by another extract made from the pituitary glands of the same species. There is some evidence, therefore, that antagonistic hormones may be produced by the same gland. In fact, in the case of the anterior pituitary we have evidence that the maturity or gonadotropic factor is associated with an antagonistic principle.

In the Welch lectures a few months ago a word of caution was given in regard to the indiscriminate use of glandular extracts—this in view of the danger of the production of a hyperantihormone state. We have now available and in use in our laboratory methods for assaying the blood serum for the presence of certain inhibitory substances. It appears to us that progress in clinical endocrinology will be more rapid as well as more certain if attention is for the time being diverted from treatment to a study of the blood of the patient so far as reliable methods are available.

THE ACTION OF IODINE IN THYROTOXICOSIS

WITH SPECIAL REFERENCE TO REFRACTORINESS

J. H. MEANS, M.D.
AND
JACOB LERMAN, M.D.
BOSTON

Eleven years has now elapsed since Plummer [1] introduced the use of iodine in the management of toxic goiter. During that entire period, iodine has been given as a routine in the Thyroid Clinic of the Massachusetts General Hospital and in some 575 cases its action has been made a matter of careful study. It is our purpose at the present time to evaluate this whole experience and to state the conclusions derived from it in the form that seems soundest to us today. We believe this a useful undertaking because it is evident that much confusion exists even now in the professional mind as to what iodine will and won't do in thyrotoxicosis.

A brief summary of the biologic facts of the problem is in order. First of all, it may be stated that, so far as is known, the sole function of the thyroid is the manufacture of thyroxine, and that in toxic goiter this function is accelerated. The cause of the acceleration is obscure. Hyperfunctioning of adenomatous tissue is a possibility; tissue that possesses the power to make the hormone but has escaped from whatever control governs the normal output of the gland. Following Plummer,[2] at one time the profession accepted as a fact that hyperfunctioning adenomas might occur in the thyroid. With the passing of time it has grown increasingly doubtful that they constitute an entity clinically separable from exophthalmic goiter. In the so-called toxic adenoma cases, if one searches the nonadenomatous portion of the gland carefully enough, one usually can find areas of ordinary hyperplasia; also it appears that these patients usually respond to iodine as do those with typical exophthalmic goiter.

Two other explanations of hyperfunction are obvious. The gland cells may be whipped up to overactivity by some stimulus from without, or they may, because of an increased rate of removal of their product, hyperfunctionate to compensate. The known facts seem to us more consistent with the latter hypothesis. It has been shown, for example, that in toxic goiter the thyroid gland is poor in organic iodine, colloid and thyroxine [3] and that the blood is abnormally rich in organic iodine and thyroxine [4] and the urine in iodine.[5] Iodine, of course, is a necessary component of the thyroxine molecule, but iodine exists in the body in other forms than as a part of this molecule. Nevertheless, the fall in thyroxine in the gland and the rise in the blood and the increased excretion of iodine in the urine suggest more rapid departure of the hormone from the gland, and the disappearance of colloid does the same, for it is in the form of iodothyroglobulin that thyroxine is stored in the acini. Thus emerges the concept of a leaking, or too porous, gland that attempts to compensate for leakage of hormone by hyperplasia and hyperfunction.[6] Another writer calls it "thyroid diarrhea." [7] We believe also that the observed clinical facts are consistent with such a theory.

What these clinical facts are can be stated quite briefly: First, our entire experience confirms Plummer's original contention that iodine brings about a rapid amelioration of the symptoms of thyrotoxicosis in toxic goiter and, accompanying this, a fall in basal metabolic rate. So constant and specific is this response that we have come to regard it as one of the cardinal manifestations of the disease. When it does not occur, we are always doubtful of the existence of thyrotoxicosis and search for some other explanation for the clinical picture. We make use of the specific response not only in treatment [8] but for diagnosis.[9] Its actual magnitude, so far as the metabolic side is concerned, is predictable with a fair degree of accuracy. It is in the neighborhood of 3.8 points of basal metabolic rate daily.

The preparation of iodine used is of no importance. Iodine is active in any form, provided the

From the Thyroid Clinic of the Massachusetts General Hospital.
Read before the Section on Pharmacology and Therapeutics at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 13, 1934.

1. Plummer, H. S.: Results of Administering Iodine to Patients Having Exophthalmic Goiter, J. A. M. A. **80:** 1955 (June 30) 1923.

2. Plummer, H. S.: The Clinical and Pathological Relationship of Simple and Exophthalmic Goiter, Am. J. M. Sc. **146:** 790, 1913.

3. Gutman, A. B.; Benedict, E. M.; Baxter, B., and Palmer, W. W.: The Effect of Administration of Iodine on the Total Iodine, Inorganic Iodine and Thyroxine Content of the Pathologic Thyroid Gland, J. Biol. Chem. **97:** 303 (July) 1932. (See particularly their figure 2.)

4. Holst, Johan; Lunde, G.; Closs, K., and Pedersen, O. C.: Ueber den inneren Jodstoffwechsel bei primären Thyreotoxikosen, Klin. Wchnschr. **7:** 2287 (Nov. 25) 1928.

5. Curtis, G. M.; Davis, C. B., and Phillips, F. J.: Significance of the Iodine Content of Human Blood, J. A. M. A. **101:** 901 (Sept. 16) 1933.

6. Holst, Johan: Die pathogenetischen Grundlagen der Thyreotoxikosetherapie, Oslo, Jacob Dybwad, 1928.

7. Harington, C. R.: The Thyroid Gland: Its Chemistry and Physiology, London, Oxford University Press, 1933.

8. Means, J. H.: The Use of Iodine in Exophthalmic Goiter, Ann. Int. Med. **4:** 117 (Aug.) 1930.

9. Means, J. H.: The Diagnostic Use of Iodine in Thyrotoxicosis, Ann. Int. Med. **7:** 439 (Oct.) 1933.

minimum effective dose or more is given. At the present time we use 10 minims (0.6 cc.) of saturated solution of potassium iodide once daily. This should be sufficient in any case.

The next important point is that the specific response will occur at any time during the course of the disease. It is not a feature merely of the onset of the malady. We have observed it taking place in characteristic form in a patient continuously thyrotoxic for eighteen years.

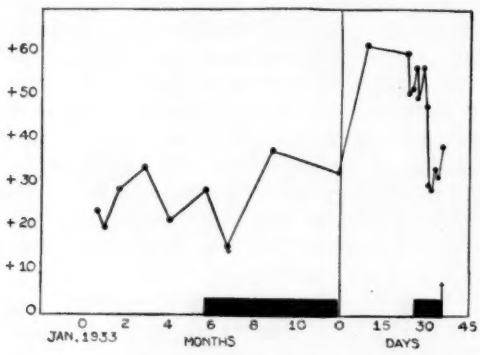

Chart 1 (case 1).—Basal metabolism chart in exophthalmic goiter, showing exacerbation during iodine administration (pseudorefractoriness) and sudden upshoot on escape from iodine control. Readministration restored basal metabolic rate to level that had been reached when iodine was stopped. The iodine administration is shown in black; the arrow denotes operation. Attention is called to the fact that the time interval is in days to the right of the perpendicular line, in months to the left.

Finally, it is our belief that iodine alters neither the duration nor the direction of progress of the disease. It merely, at any one moment, holds in abeyance a portion of its symptoms. This conception is not susceptible of proof, but our clinical experience makes us feel that its being correct is very probable.

One is next led to inquire in what way this specific response to iodine is brought about, and this question is intimately involved with that of refractoriness. It is the experience, doubtless, of all who give iodine to thyrotoxic patients that if the drug is continued the patients will often get worse in spite of it. Is this because the drug has become ineffectual and no longer capable of exerting an influence on thyroxine discharge or is it because the disease, entering a more severe stage, produces an intensification of symptoms in spite of a continued iodine control? One must bear in mind that control of symptoms by iodine is to be looked on as partial or relative, not total or absolute. Failure to grasp this fact is responsible for some of the existing differences of opinion about refractoriness.

Whether true refractoriness in the sense of cessation of drug action exists is difficult to determine. It has seemed to us that the behavior of the patient on stopping the drug is the chief source of evidence. Should a patient getting worse on iodine become refractory to iodine, one would expect that no great change in symptoms or direction of metabolic trend would occur on the omission of the drug. On the other hand, under the same circumstances should iodine be yet exerting some control, one would expect an intensification of the symptoms and an abruptly steeper upward trend of the basal metabolic rate. The patient, though getting worse on iodine, would get worse at a still faster pace on its omission, provided the drug was exerting some influence.

Scrutiny of our cases leads us to believe that the latter is what actually happens and to conclude, therefore, that so-called refractoriness to iodine is apparent, not real. The point is one of more than academic interest, because the therapeutic program depends on it. If a patient became truly refractory to iodine, the indication would be to stop the drug for a time and later resume its administration. If, on the other hand, there is no such thing as true refractoriness, iodine should be maintained steadily until thyroidectomy is performed. In 1917 Means and Aub[10] called attention to the fact that a rising basal metabolic rate in toxic goiter indicates that surgery may be hazardous and that a rising metabolism constitutes a positive indication for the postponement of operation. This was in preiodine days. The principle, however, holds good now as well as then. Therefore the practical question comes up occasionally when one has a patient in the hospital, fully iodinized yet getting worse, of what shall be done with him. Shall he be taken off iodine or left on it? We believe he should be kept on. Nothing is gained by taking him off and he is allowed to run a greater risk of death from thyrotoxicosis by so doing. Our procedure would be to follow a policy of watchful waiting with iodinization maintained. When a plateau had been reached, if not at too high a level, we should advise operation. Following such a course, we believe that the risk of toxic crisis or storm is minimized. Allowing escape from iodine control at a high level is definitely running the risk of storm.

Two cases will serve to illustrate these points:

CASE 1.—Phyllis A., aged 19 years, with recurrent thyrotoxicosis (exophthalmic goiter), had a basal metabolic level in the neighborhood of plus 25. Under iodine it dropped slightly (chart 1), then rose again, although iodine was continued. One might say that she had become refractory to iodine. This is not true, however, for on the omission of iodine there is a very rapid rise in basal metabolic rate to a new high level of plus 60 and intensification of symptoms. On the readministration of iodine she returns to precisely the metabolic level which

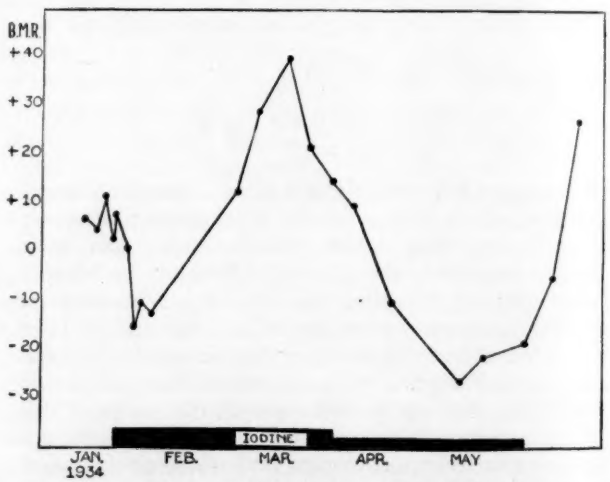

Chart 2 (case 2).—Basal metabolism chart in exophthalmic goiter. At the left a positive diagnostic test with iodine is shown and then an exacerbation and remission, both occurring during maintained iodinization. The iodine administration is shown in black.

she left on cessation of iodine. We have observed this sort of thing in other cases and believe that it represents the rule. Of course, ordinarily we do not omit iodine because, as already stated, we believe it undesirable from the patient's point of view to do so.

CASE 2.—Beatrice H., aged 17 years, had a metabolic rate within the normal zone. There was a firm and somewhat

10. Means, J. H., and Aub, J. C.: A Study of Exophthalmic Goiter from the Point of View of the Basal Metabolism, J. A. M. A. 69: 33 (July 7) 1917.

irregular thyroid with palpable thrill and bruit and very questionable thyrotoxic symptoms. There were no eye signs. Iodine was given for diagnostic purposes, and, as seen in chart 2, there was a prompt fall to a basal metabolic level in the neighborhood of minus 12 (from one of about plus 7). This is to be regarded as a positive test ruling in thyrotoxicosis. Subsequent events prove its trustworthiness. The patient was continued on iodine and in spite of it the basal metabolic rate continuously rose till it reached plus 40, and the symptomatology became typical. In other words, a classic exophthalmic goiter was developing under our eyes in a fully iodinized patient. This might be interpreted as refractoriness, but, we believe, not correctly. The next chapter is that as iodine is further continued the metabolism again falls clear to a new low level of minus 23, and the symptoms improve. Had iodine been omitted in the middle of March and resumed early in April, one would seemingly have had a perfect case for refractoriness. We believe, however, that the truth of the matter is that iodine has continuously exerted an effect in this case and that the curve indicates a spontaneous exacerbation and remission taking place in spite of iodine, but at a lower level than would have obtained if no iodine had been used. The proof of this is the final event, namely, that when iodine is at last omitted, back comes the disease full-blast. This is another form of the diagnostic use of iodine: intensification of symptoms on omission instead of amelioration on giving the drug.

Addendum.—After this paper was prepared, certain additional data of importance were secured in case 2. The last metabolic rate determination shown in chart 2 was plus 27 per cent on June 6. For two months it fluctuated about plus 20, off iodine. August 4, iodine was given again. The metabolism promptly fell to minus 3 on August 11, and on August 12 the patient had a subtotal thyroidectomy. This added information confirms the opinion expressed in the paper that the rapid rise on cessation of iodine, beginning March 19, was due to escape from iodine control, and that the slower rise in the months of January, February and March, on iodine, was due to a natural intensification of the disease.

In 1931 our colleagues Drs. W. O. Thompson and Phebe K. Thompson [11] published the reports of a group of cases, some from the Massachusetts General Hospital, some from the Presbyterian Hospital in Chicago, which they believed showed refractoriness. We have studied these data rather carefully. In each case the omission of iodine is followed by a steeper upward trend of the metabolic curve. Therefore we believe that the interpretation of refractoriness is not entirely sound. In short, it seems to us that the thyrotoxic patient fails to respond to iodine only when he is already under its influence. On the omission of iodine a certain time, from two to three weeks perhaps, must elapse before a maximum response again can be had. This, we believe, is simply because it takes some such time for the effect of previous iodine to wear off or for the patient to escape fully from iodine control. He cannot respond to a second course of iodine until he has escaped from the influence of his first. The occasional apparent lack of response to iodine can be explained by the assumption that the drug was given at a time when the intensity of the intoxication was increasing. The effect of iodine under such circumstances might be merely to hold things level for a time.

It may be permissible to show again a diagram published some years ago,[12] which we still find consistent with what we observe clinically. It indicates simply that thyrotoxicosis runs its course, irrespective of iodine control, but that at any one time the intensity of intoxication is less if the patient is under iodine control than if he is not. At any stage of the disease the effect of giving iodine will be to drop the intensity of thyrotoxicosis from the upper curve to the lower, and, of omitting it, the reverse.

How, now, may one relate all this to the morbid physiology of the thyroid? We mentioned the appeal of the concept of a leaking gland. A plausible explanation of the action of iodine is that raising its concentration in the blood in part dams back the leak. The follicles fill up with colloid and the abnormally rapid escape of hormone is partly checked. When iodine is withdrawn, out it spills again.

The production of thyrotoxicosis by means of iodine, the so-called iod-Basedow of the Germans, is difficult to reconcile with such a theory. We are very doubtful, however, of the existence of iod-Basedow, having never ourselves seen any convincing evidence of it. Furthermore, we have the word of one competent European investigator, Professor Dautrebande of Liége,[13] that cases diagnosed iod-Basedow seen by him have responded to iodine in the usual manner. This certainly throws great doubt that iodine in the first place produced their thyrotoxicosis.

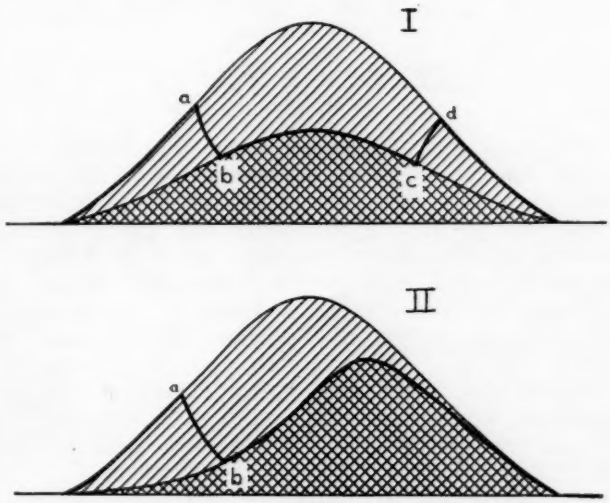

Chart 3.—Schematic representation of iodine relationships in toxic goiter. The curves represent the totality of thyrotoxicosis. The upper curve in each graph is the course that would be followed if no iodine was ever given; the lower, the course that would be followed if iodine should be given throughout. The duration of the disease, it will be noted, is not affected by iodine, nor is its direction of progress, merely its intensity. The effect of giving iodine at any moment will be to drop the intoxication from the upper to the lower curve, as from *a* to *b*; that of omitting iodine, the reverse, as from *c* to *d*. Graph II is added to indicate that the curve of full iodinization and that of no iodinization may not always be precisely parallel.

CONCLUSIONS

1. The clinical facts regarding iodine in thyrotoxicosis are that it produces an altogether characteristic and specific response, which consists in an amelioration of symptoms and a drop in metabolic rate. This response will occur at any stage of the disease.

2. It appears that the response has no relation to the duration or direction of progress of the disease but merely acts as a check on the intensity of its symptoms.

3. These clinical facts are consistent with the theory that in thyrotoxicosis the thyroid allows the escape of thyroxine to proceed at an excessive rate; to leak, in fact, and that the cells of the thyroid hyperfunction in consequence. Iodine, it is suggested, sets up a tem-

11. Thompson, W. O., and Thompson, Phebe K.: Exophthalmic Goiter: The Development of Refractoriness to Iodine, Arch. Int. Med. **48**: 351 (Sept.) 1931.

12. Means, J. H.; Thompson, W. O., and Thompson, Phebe K.: On the Nature of the Iodine Reaction in Exophthalmic Goiter, with Particular Reference to the Effect of Iodine Late in the Course of the Disease, Tr. A. Am. Physicians **43**: 146, 1928.

13. Dautrebande, L.: Personal communication to the authors.

porary obstacle to this excessive outflow: it checks the leakage of thyroxine from the gland. The known facts of iodine and thyroxine content of the gland, blood and urine are consistent with such a theory.

4. We believe that so-called refractoriness is apparent, not real. Thyrotoxic patients who are unaffected by iodine are those who are already fully iodinized.

5. We doubt the existence of so-called iod-Basedow.

6. The iodine response is valuable in the management of toxic goiter, both in treatment and in diagnosis, but its fundamental nature must be familiar if it is to be used successfully.

THE PHARMACOLOGY OF THE THYROID IN MAN

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Although more is known about the thyroid than about any other gland of internal secretion, many important problems concerning its physiology and pharmacology remain unsolved. For example, very little is known about the mechanism of the action of thyroxine, and more precise information should be obtained about the form or forms in which iodine occurs in the gland, the mechanism of the action of iodine in exophthalmic goiter, and the relationship between the thyroid and other glands of internal secretion, notably the pituitary. It was with the idea of throwing some light on these problems that the present series of observations was undertaken.

THE RATE OF FORMATION OF THYROXINE

Boothby and his co-workers [1] and we ourselves [2] have shown that about 0.25 mg. to 0.35 mg. of thyroxine must be injected intravenously every day in order to maintain the basal metabolism of patients with marked myxedema at the normal level. In such patients there is little or no functioning thyroid tissue and this figure of about 0.3 mg. (0.2 mg. of iodine) daily is the nearest approach that can be made at present to the rate of formation of thyroxine or its equivalent by the normal thyroid gland. At this rate, in three score years and ten the thyroid of a normal individual would produce about 7.8 Gm. of thyroxine. From the maintenance dose of thyroxine and the effect of 10 mg. given intravenously in myxedematous man, we have calculated that there are about 10 to 14 mg. in the body of a normal individual outside of the thyroid gland, a figure almost the same as that previously arrived at by Plummer [3] and Boothby.[4] If the figure for the rate of production of the thyroid hormone is approximately correct, then the iodine requirement of the normal thyroid may be about 0.2 mg. a day, and the amount of iodine supplied on the average to an individual in this country in the form of iodized salt (approximately 1.0 mg. each day) is probably more than adequate for the prevention of simple goiter.

THE EFFECT OF THYROXINE

The intravenous administration of 10 mg. of thyroxine produces about seven times as much effect when given to a patient whose basal metabolism is minus 40 per cent as when given to a patient with a normal level of metabolism.[5] The duration of the effect both clinically and metabolically at the low level of metabolism is remarkable. Thus, 10 mg. at this level raises the metabolism about 32 points on the average in from three to ten days and the effect on metabolism persists for from seventy to eighty days. Beginning about twenty-four to forty-eight hours after the injection is a period of intoxication, which lasts for from two to three weeks but is particularly marked during the first week and is characterized by aching and marked tenderness of the muscles, falling out of the hair and peeling of the skin. During the first few days there is often fever (the temperature sometimes rising as high as 104 F.), occasionally nausea and rarely vomiting. The period of improvement, which overlaps the period of intoxication, begins a few days after the injection is given and gradually reaches a maximum about four to six weeks after the administration, when the metabolism has already fallen considerably. In other words, the maximum clinical improvement following a single dose does not coincide with the maximum increase in metabolism. When the metabolism finally returns to its original level in from two to three months after treatment, the patient is still alert and usually does not appear very myxedematous. Often the body weight is less than before the injection was given. The full blown picture of myxedema develops only after the metabolism has persisted at the level of minus 40 per cent for many weeks, and in some instances for many months.

Because of the initial period of intoxication that follows the administration of a single large dose of thyroxine or of desiccated thyroid, and the fact that improvement in a patient with myxedema occurs only slowly, the ideal method of treatment is to raise the metabolism gradually by slowly increasing doses until the minimum amount is being administered that will maintain the basal metabolism at the normal level. In this way unpleasant symptoms are avoided. In particular, sudden changes in metabolism are to be avoided in patients with heart disease, notably those with angina pectoris. In patients with myxedema who are desperately ill there is great danger of death from large doses because of the period of intoxication and the slowness with which beneficial effects appear. They are unable to tolerate the sudden replacement of the very thing that their bodies lack. In the treatment of all patients with myxedema it should be remembered that adjust-

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1. Boothby, W. M.; Sandiford, Irene; Sandiford, K., and Slosse, J.: The Effect of Thyroxine on the Respiratory and Nitrogenous Metabolism of Normal and Myxedematous Subjects: I. A Method of Studying the Reserve or Deposit Protein with a Preliminary Report of the Results Obtained, Tr. A. Am. Physicians **40**: 195, 1925.

2. Thompson, W. O.; McLellan, L. L.; Thompson, Phebe K., and Dickie, Lois F. N.: The Rates of Utilization of Thyroxine and of Desiccated Thyroid in Man: The Relation Between the Iodine in Desiccated Thyroid and in Thyroxine, J. Clin. Investigation **12**: 235 (Jan.) 1933.

3. Plummer, H. S.: Interrelationship of Function of the Thyroid Gland and of Its Active Agent, Thyroxine, in the Tissues of the Body, J. A. M. A. **77**: 243 (July 23) 1921.

4. Boothby, W. M.: The Thyroid Problem, Collected Papers of the Mayo Clinic **20**: 495, 1928.

5. Thompson, W. O.; Thompson, Phebe, K.; Brailey, A. G., and Cohen, A. C.: The Calorigenetic Action of Thyroxine at Different Levels of Basal Metabolism in Myxedema, J. Clin. Investigation **7**: 437 (Aug.) 1929.

ment to any dose may require many months, and changes should be made slowly.

IMPORTANCE OF THE PECULIAR CONFIGURATION OF THE THYROXINE MOLECULE

The marked reduction in the calorigenic activity of thyroxine produced by making slight changes in the molecule may be seen from chart 1. We have extended our previous observations [6] and have noted that in a patient with myxedema the intravenous administration of 8.6 Gm. of diiodotyrosine in sixteen injections over a period of eighteen days produced an increase in basal metabolism from minus 36 per cent to minus 26 per cent and a loss of 2.4 Kg. If this represents a true change, the effect per millimol was only about one ten thousandth that of thyroxine.

If a phenol group is added to the diiodotyrosine molecule with the formation of a diphenyl ether group, diiodothyronine is produced. This compound represents thyroxine with two atoms of iodine removed from the molecule. Diiodothyronine has a much greater calorigenic action than diiodotyrosine. Thus, in one patient with myxedema 100 mg. intravenously raised the metabolism from minus 36 per cent to minus 21 per cent and, in another, 150 mg. raised it from minus 42 per cent to minus 22 per cent. This suggests that the presence of the diphenyl ether group is important. It is of interest to note the rather rapid return of the basal metabolism to the premedication level following the administration of diiodothyronine (seven and eight days respectively in two patients) compared with the slow return following the administration of thyroxine (from seventy to eighty days). Thus the removal of two atoms of iodine from the thyroxine molecule not only greatly reduces the efficacy of the compound in raising metabolism but also appears to alter the nature of the metabolic response.

If the remaining two atoms of iodine are removed to form thyronine or desiodothyroxine, the calorigenic activity is still further reduced. We have given 228 mg. intravenously over a period of five days to one patient with myxedema and 400 mg. intravenously in two days to another without any clear-cut effect on metabolism. These observations with thyronine and diiodothyronine show the importance of the iodine in the thyroxine molecule.

It is of interest to observe the effect of altering the amino group in the molecule. To do this, one of us (S. B. N.) has prepared N-acetyl thyroxine according to the method of Kendall and Osterberg.[7] In this compound one of the hydrogen atoms of the amino group is replaced by an acetyl group. The acetyl group is comparatively stable and only slowly hydrolyzed. The intravenous administration of this substance in a dose of 31.5 mg. produced only a slight but fairly prolonged increase in metabolism (from minus 41 to minus 35 per cent). When administered subcutaneously suspended in 10 per cent dextrose the effect was greater, 10.5 mg. producing an increase in metabolism from minus 38 to minus 29 per cent in one patient and 21.0 mg. an increase from minus 29 to minus 17 per cent in another. In both instances the effect was prolonged and in this respect resembled that of thyroxine. The prolonged calorigenic action of thyroxine and N-acetyl thyroxine (each containing four iodine atoms) compared with the much shorter action of diiodothyronine (containing only two) suggests that the prolonged effect of thyroxine may be dependent on the presence in the molecule of all four iodine atoms. It would also appear that substitution of one hydrogen atom of the amino group of thyroxine with a stable acetyl group yields a product (N-acetyl thyroxine) possessing very much less calorigenic activity.

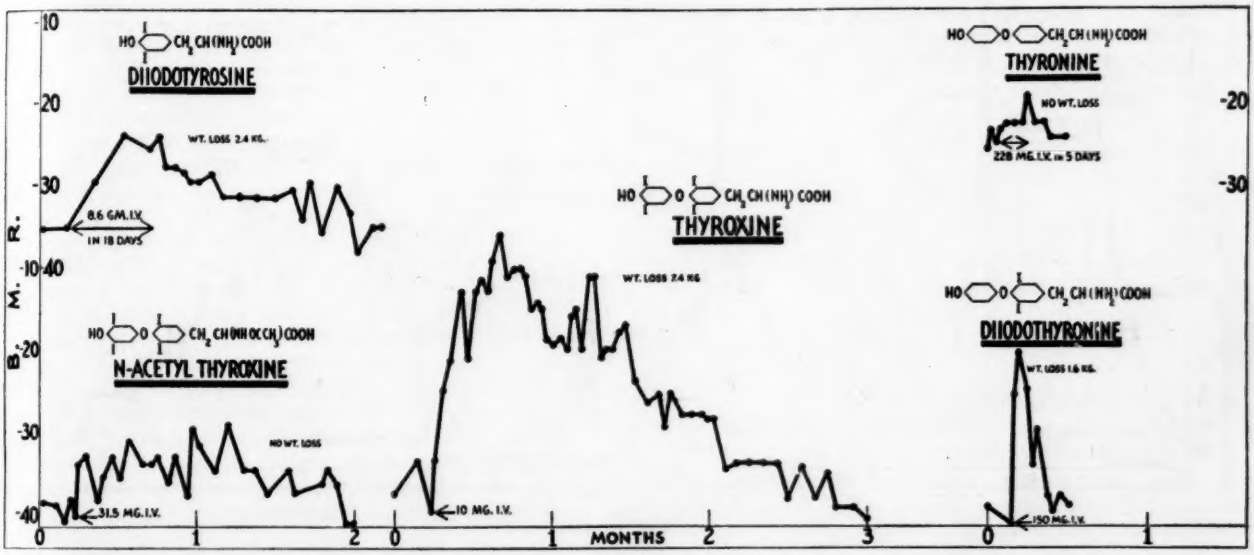

Chart 1.—Effect of alterations in the thyroxine molecule. All four iodine atoms, amino and diphenyl ether groups essential for maximum activity; removal of two iodine atoms completely alters nature of metabolic response.

These observations with various derivatives of thyroxine emphasize the importance of preserving the integrity of the thyroxine molecule if its maximum effect is to be produced.

DINITROPHENOL

Observations on the calorigenic action of alpha-dinitrophenol (1-2-4) ($C_6H_3(NO_2)_2OH$) have recently been reported by Cutting, Tainter and others [8] in this country and by Magne,

6. Thompson, W. O.; Alper, J. M.; Thompson, Phebe K., and Dickie, Lois F. N.: The Effect of Diiodotyrosine on the Basal Metabolism in Myxedema, J. Clin. Investigation **13**: 29 (Jan.) 1934.

7. Kendall, E. C., and Osterberg, A. E.: The Chemical Identification of Thyroxine, J. Biol. Chem. **40**: 265 (Dec.) 1919.

8. Cutting, W. C., and Tainter, M. L.: Proc. Soc. Exper. Biol. & Med. **29**: 1268 (June) 1932. Cutting, W. C.; Mehrtens, H. G., and Tainter, M. L.: Actions and Uses of Dinitrophenol, J. A. M. A. **101**: 193 (July 15) 1933. Tainter, M. L.; Stockton, A. B., and Cutting, W. C.: Use of Dinitrophenol in Obesity and Related Conditions, ibid. **101**: 1472 (Nov. 4) 1933.

Mayer, Plantefol and others[9] in France. According to Dodds and Pope,[10] 3:5 dinitro-orthocresol is about three times as effective in the guinea-pig. In chart 2 it may be seen that after a single large dose of dinitrophenol the effect on metabolism becomes maximum in a few hours, in comparison with from three to ten days after a single large dose of thyroxine. After a single intravenous injection of 150 mg. of diiodothyronine the effect becomes maximum in about two days, but, as in the case of dinitrophenol, the effect on metabolism disappears in a few days, although the effect is slightly more prolonged than that of dinitrophenol. Unlike thyroxine, dinitrophenol appears to have about the same effect on metabolism regardless of the level before treatment. There is only a slight effect on the pulse rate and a virtual absence of the initial period of intoxication that follows the administration of thyroxine. In patients with myxedema in doses sufficient to raise the basal metabolism to normal there is little effect on body weight or clinical condition, although a few notice a slight increase in their sense of well being and slight muscle pain. Thus a patient may continue to be myxedematous although the metabolism is raised from minus 40 per cent to normal. When the rate is raised to about 50 per cent above normal there is some flushing of the skin, an increased sense of warmth and often the patient feels better, whereas an equal increase in metabolism produced by thyroxine would make the patient very uncomfortable. The increased urinary excretion of nitrogen that follows the administration of thyroxine is said to be absent following the administration of dinitrophenol.[11] From these observations it is apparent that the increased metabolism produced by thyroxine is different from that produced by dinitrophenol. It is interesting that the latter exerts its marked calorigenic effect in spite of the fact that its molecule contains only one benzene ring and no iodine. Although dinitrophenol may produce pharmacologic rather than physiologic effects, its marked action in the absence of thyroid function suggests that the basal metabolism may be altered by more than one mechanism.

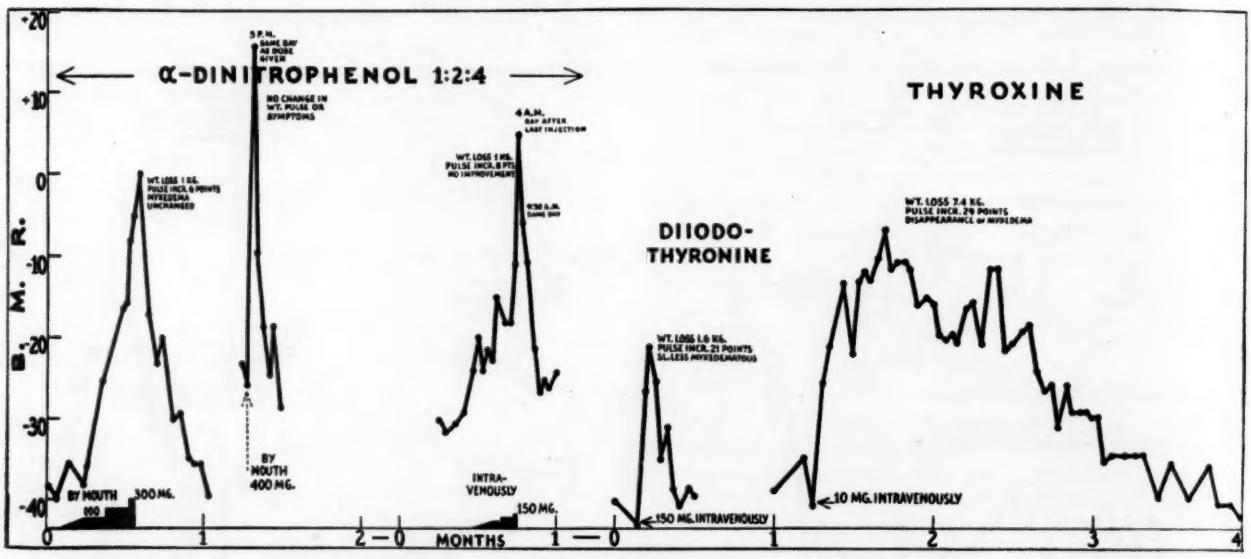

Chart 2.—Dinitrophenol compared with diiodothyronine and thyroxine. Rapid rise and fall of metabolism after dinitrophenol, somewhat similar to that after diiodothyronine but in marked contrast to slow rise and fall after thyroxine.

THE EFFECT OF ADMINISTERING THYROXINE IN VARIOUS FORMS BY MOUTH

Until recently it was thought that thyroxine had no effect by mouth, but it is now known that while it has only a slight effect as the free amino acid, it has a well marked effect when given in an alkaline solution, which is about 63 per cent as great as its effect when given intravenously in the same form.[12] It was thought that this well marked effect of an alkaline solution might be due to the formation of the disodium salt. This salt was therefore made by one of us (S. B. N.) according to the method of Kendall[13] and had much less effect than an alkaline solution, possibly because of partial hydrolysis into sodium hydroxide and thyroxine.[14] Its effect was, indeed, about the same as that of the monosodium salt in crystalline form, which in turn was about 25 per cent as great as that of thyroxine given intravenously. The free amino acid suspended in distilled water has only about one one hundred and fiftieth as much effect as thyroxine given intravenously.

This augmentation by the action of alkali seen in the case of thyroxine is also noted in the case of a peptide of thyroxine[15] prepared by proteolytic digestion of desiccated thyroid according to the method of Harington and Salter.[16] When suspended in distilled water and administered by mouth it produced only about 28 per cent as much increase in basal metabolism as thyroxine given intravenously, or almost exactly the same effect as monosodium thyroxine. This means that the peptide had nearly forty times as much effect per milligram of iodine as thyroxine given in the form of the free amino acid, suggesting that the combination of thyroxine with another amino acid in some way increases its absorption, possibly by facilitating the ease with which it forms a soluble salt in the small intestine. When the peptide was given by mouth in alkaline solution, its effect was approximately three times as great as when it was given in suspension and slightly greater than that of thyroxine in alkaline solution. In contrast to these

9. Magne, H.; Mayer, A.; Plantefol, L., and others: Ann. de physiol. **8**: 1, 1932.
10. Dodds, E. C., and Pope, W. J.: Dinitro-o-Cresol as a Stimulator of Metabolism, Lancet **2**: 352 (Aug. 12) 1933.
11. Cutting, W. C., and Tainter, M. L.: Metabolic Actions of Dinitrophenol with the Use of Balanced and Unbalanced Diets, J. A. M. A. **101**: 2099 (Dec. 30) 1933.
12. Thompson, W. O.; Thompson, Phebe K.; Dickie, Lois F. N., and Alper, J. M.: Effect of Alkali on the Absorption of Thyroxine from the Gastro-Intestinal Tract, with a Note on the Comparative Effects of Synthetic and "Natural" Thyroxine Injected Intravenously, Arch. Int. Med. **52**: 809 (Nov.) 1933.
13. Kendall, E. C.: Chemistry of the Thyroid Secretion, Harvey Lectures, Series 15, 1919-1920, p. 41.
14. Thompson, W. O.; Nadler, S. B.; Taylor, S. G., and Thompson, Phebe K.; Recent Observations on Thyroxine and Allied Compounds, Proc. Soc. Exper. Biol. & Med. **31**: 1000 (May) 1934.
15. Thompson, W. O.; Nadler, S. B.; Thompson, Phebe K., and Dickie, Lois F. N.: The Effect of Alkali on the Absorption of a Peptide of Thyroxine from the Gastro-Intestinal Tract, J. Clin. Investigation **13**: 933 (Nov.) 1934.
16. Harington, C. R., and Salter, W. T.: The Isolation of l-Thyroxine from the Thyroid Gland by the Action of Proteolytic Enzymes, Biochem. J. **24**: 456, 1930.

results with thyroxine and thyroxine peptide, alkali did not have a clear-cut effect on the absorption of an acid-insoluble precipitate from a peptic digest[17] of desiccated thyroid. Thus the effect of thyroxine was augmented most, that of the peptide less and that of the acid-insoluble preciptate not significantly. In other words, as the complexity of the molecule increased, the effect of alkali decreased.

IODINE IN RELATION TO THE CALORIGENIC ACTIVITY OF DESICCATED THYROID

Hunt and Seidell,[18] Means, Lerman and Salter[19] and we ourselves[2] reported observations which suggested that the activity of desiccated thyroid was proportional to its total iodine content. On the other hand, Harington and Randall[20] isolated diiodotyrosine from the thyroid by alkaline hydrolysis and by the action of proteolytic enzymes and concluded that at least 50 per cent of the total iodine was present in this form. Since diiodotyrosine possesses little calorigenic activity, there was a discrepancy between clinical observations on the one hand and chemical on the other. It is possible that the finding on the part of all three groups of investigators that activity is proportional to total iodine may have been a coincidence and that the problem may be more complex.

Our original conclusion was based on the observation that in each of two patients with myxedema the amounts of desiccated thyroid and of thyroxine that had to be given orally and intravenously respectively every day in order to hold the basal metabolism at normal contained the same total amounts of iodine. When we began to compare the effects of single large doses of the two substances we noticed that the effect of a certain lot of desiccated thyroid was on the average only 62 per cent as great as that of thyroxine given intravenously and that the ratio of the effects of the two substances varied greatly from patient to patient.[21] Moreover, comparison of the maintenance doses in the same patient showed that certain lots of sheep and beef thyroid had less effect than a lot of hog thyroid in doses containing the same total amounts of iodine.

The next logical step was to attempt to isolate from desiccated thyroid an iodine fraction that would possess most of the calorigenic activity. After digestion of desiccated thyroid with pepsin for seventy-two hours, most of the calorigenic activity is possessed by the acid-insoluble portion, which represents (in the lot used) only about 45 per cent of the total iodine. Data thus far collected suggest that, per milligram of iodine the effect of the acid-insoluble precipitate is greater than that of the desiccated thyroid from which it was prepared, but because of the disproportionate effects of increasing doses it is impossible at the present time to make quantitative comparisons.[22]

The activity of a given amount of desiccated thyroid is usually slightly greater than that of the acid-insoluble portion derived from it, a discrepancy that may be explained by a slight calorigenic activity of the acid-soluble portion,[23] which has been reported by Lerman and Salter[24] to possess no calorigenic activity. The curves denoting the changes in metabolism following single large doses of the acid-soluble portion appear to be different from those for the acid-insoluble portion, being characterized by a more rapid return to the level before treatment. Lerman and Salter[24] report that after digestion with pepsin for seventy-two hours desiccated thyroid loses about half of its activity and that the effect of the acid-insoluble portion is the same per milligram of iodine as that of the desiccated thyroid from which it is prepared. They therefore conclude that although diiodotyrosine is inert it "exerts calorigenic action when given in its natural chemical combination with thyroxine in the form of whole gland." It is impossible to state at the present time whether different methods of assay account for the differences in results.

EFFECT OF HEATING WITH ALKALI ON DESICCATED THYROID AND THYROXINE: BEARING ON METHODS OF STANDARDIZATION OF DESICCATED THYROID

We have observed[22] that, after heating with approximately normal sodium hydroxide on a water bath for four hours, desiccated thyroid loses more than two thirds of its calorigenic activity. No activity is lost if the mixtures are not heated. When thyroxine is heated with alkali in the same manner, its effect is not altered. Cameron and Carmichael,[25] on the basis of the rate of growth and hypertrophy of organs in rats, concluded that hydrolysis with sodium hydroxide destroyed at least two thirds of the activity of iodothyroglobulin. Regardless of the explanation of these observations, it becomes apparent at once that the method used by all investigators for isolation of the active principle from the thyroid, namely, hydrolysis with alkali, destroys most of the gland's activity. Indeed, the low yield of crystalline thyroxine from desiccated thyroid has always been one of the most serious handicaps to a systematic study of its properties and may be attributed either to destruction of thyroxine or to the presence of only a small quantity of iodine in the form of thyroxine to begin with.

The effect of heating desiccated thyroid with alkali has an important bearing on the suggestion advanced by Harington and Randall[26] and by Gutman, Benedict, Baxter and Palmer[27] that for pharmaceutic purposes desiccated thyroid should be standardized in terms of thyroxine iodine rather than in terms of total organic iodine. Using guinea-pigs for assay, Gutman and his co-workers found calorigenic activity proportional to thyroxine rather than to total iodine. The assay methods of Hunt[18] and Gudernatsch,[28] which depend on the effect of thyroid on the susceptibility of white mice to acetonitrile and on the metamorphosis of tadpoles respectively, are certainly no more accurate than the total iodine method and have indeed led to the conclusion that activity is proportional to total iodine. Biologic assay on patients with myxedema is accurate but too time consuming to be practical, requiring as it does many months to standardize a single preparation. In many instances the determination of total organic iodine is probably satisfactory for clinical purposes. At present the glands used by several American manufacturers for the preparation of their desiccated thyroid

17. We are indebted to Dr. Klein of the Wilson Laboratories for enzymes and desiccated hog thyroid supplied for these experiments.

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19. Means, J. H.; Lerman, J., and Salter, W. T.: The Rôle of Thyroxine Iodine and Total Organic Iodine in the Calorigenic Action of Whole Thyroid Gland, J. Clin. Investigation **12**: 683 (July) 1933.

20. Harington, C. R., and Randall, S. S.: Observations on the Iodine Containing Compounds of the Thyroid Gland: Isolation of dl-3:5 Diiodotyrosine, Biochem. J. **23**: 373, 1929; Isolation of dl-3:5 Diiodotyrosine from the Thyroid Gland by the Action of Proteolytic Enzymes, ibid. **25**: 1032, 1931.

21. Thompson, W. O.; Thompson, Phebe K.; Taylor, S. G., and Dickie, Lois F. N.: The Calorigenic Action of Single Large Doses of Desiccated Hog Thyroid: Comparison with That of Thyroxine Given Orally and Intravenously, Arch. Int. Med. **54**: 888 (Dec.) 1934.

22. A preliminary report of this work was made at the meeting of the American Society for Clinical Investigation in Atlantic City, N. J., April 30, 1934, by Thompson, W. O.; Nadler, S. B.; Taylor, S. G., and Thompson, P. K.; J. Clin. Investigation **13**: 690 (July) 1934.

23. Thompson, W. O.; Thompson, P. K.; Taylor, S. G. III; Nadler, S. B., and Dickie, L. F. N.: Compounds That Affect the Basal Metabolism in Man, Endocrinology, to be published.

24. Lerman, J., and Salter, W. T.: The Calorigenic Action of Thyroid and Some of Its Active Constituents, Tr. Am. A. Study of Goiter, 1933, p. 160.

25. Cameron, A. T., and Carmichael, J.: An Attempt to Evaluate Thyroid Preparations Utilizing Their Effect on Growth Rate and Production of Organ Hypertrophy in the Young White Rat, Tr. Roy. Soc. Canada **20**, sect. 5, 1926, p. 1.

26. Harington, C. R., and Randall, S. S.: The Chemical Assay of Thyroid Gland, Quart. J. Pharm. & Pharmacol. **2**: 501 (Oct.-Dec.) 1929.

27. Gutman, A. B.; Benedict, E. M.; Baxter, B., and Palmer, W. W.: The Effect of Administration of Iodine on the Total Iodine, Inorganic Iodine and Thyroxine Content of the Pathological Thyroid Gland, J. Biol. Chem. **97**: 303 (July) 1932.

28. Gudernatsch, J. F.: Feeding Experiments on Tadpoles: I. The Influence of Specific Organs Given as Food on Growth and Differentiation: A Contribution to the Knowledge of Organs with Internal Secretion, Arch. Entwcklngsmechn. d. Organ. **35**: 457, 1912.

contain fairly high concentrations of iodine, and in normal glands with high iodine contents Gutman and his associates have found the relation between total organic iodine and thyroxine iodine to be fairly constant. They have also shown that the relationship between the two is much more constant in preparations of desiccated thyroid that conform to United States Pharmacopeia requirements than those which do not.[29] As long as the U. S. Pharmacopeia requirements are adhered to, similar results may frequently be obtained whether total organic iodine or thyroxine iodine is used for standardization. Nevertheless there is still room for a method of standardization that meets the most rigid chemical and metabolic standards. Such a method may depend on the determination of a certain fraction of the total iodine which possesses nearly all the calorigenic activity, but it must not destroy activity. Until such a method is adequately worked out and its reliability proved beyond question, it would probably be unwise for the United States Pharmacopeia to change its requirements.

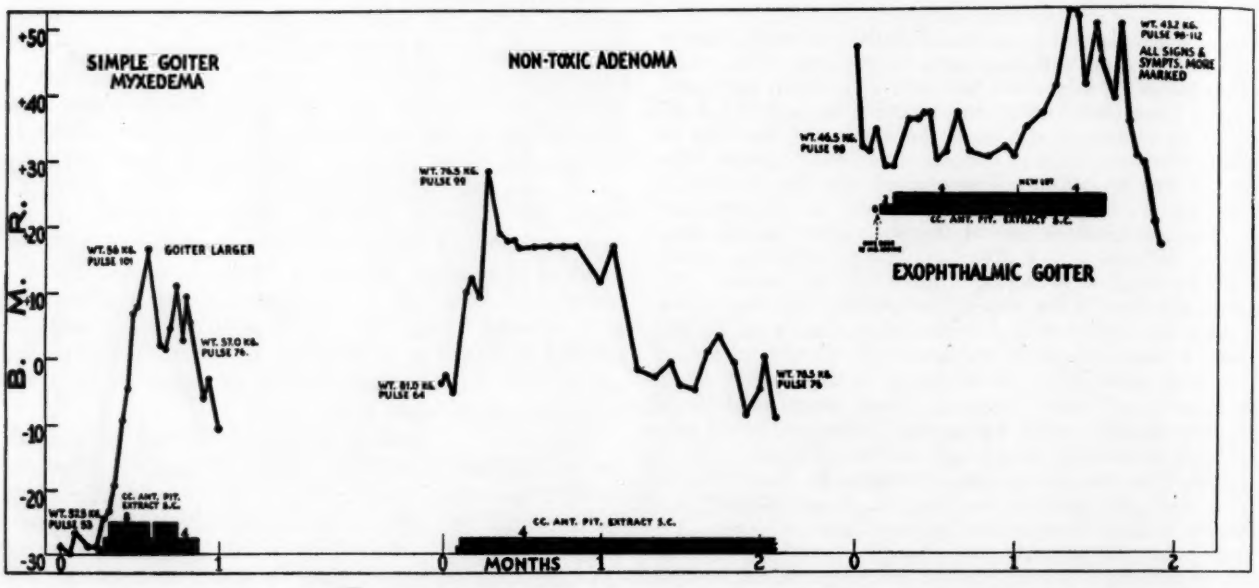

Chart 3.—Calorigenic action of anterior pituitary. Mild myxedema improved; nontoxic adenoma made toxic; exophthalmic goiter made worse.

Since no method has been demonstrated to yield with certainty the percentage of iodine present as thyroxine, the adoption of the thyroxine content as a method of standardization by the British pharmacopeia may seem a little premature. The need for an accurate method is obvious. It is hardly necessary to stress what Hunt has already pointed out; namely, that the statement that a patient has had a certain number of grains of thyroid in a given time is of little value.

IODINE REACTION

The precise nature of the iodine reaction[30] in exophthalmic goiter still remains a mystery. We have found that, in exophthalmic goiter in Boston, 6 mg. of iodine a day is about the minimum amount that will produce a maximum reduction in basal metabolism,[31] and in Chicago the amount is between 6 and 12 mg., although the exact figure is still to be determined. Other pertinent facts about the iodine reaction are that: 1. The reaction may be reversible;[32] i. e., the metabolism may rise and the severity of the disease increase during the administration of inadequate doses of iodine (from 0.75 to 3 mg. daily) and show a well marked reduction during the immediate subsequent administration of much larger doses (250 mg. daily). 2. The iodine must be administered at a certain minimum rate in order for the effect to be maximum; i. e., administration of 3 mg. daily for fourteen days will not produce the same amount of reduction on the average as the administration of 6 mg. daily for seven days. 3. Patients may be initially refractory to iodine or may become refractory after an initial response during its continuous administration.[33] 4. The same patient may show remissions and relapses in the disease when iodine is administered[34] continuously and when it is not administered at all. 5. Refractoriness to iodine may disappear after iodine has been omitted for four weeks.[33] 6. During the development of refractoriness, the minimum amount of iodine necessary to produce a maximum reduction in basal metabolism may increase.[33] 7. A dose of iodine which in itself is too small to cause a reduction in the rate of basal metabolism may interfere with the effect of much larger doses administered immediately after ward.[32] 8. Although the rate of metabolism may not show an initial reduction while iodine is being administered, it may rise markedly after omission of iodine. 9. While the usual effect of iodine is to force the gland to store colloid, in some instances the iodine content of the gland remains low in spite of the administration of large doses of iodine before operation.[27] 10. Hypothyroidism may develop during the administration of iodine in either the preoperative[34] or the postoperative[35] periods. 11. Iodine does not appear to prevent regeneration of thyroid tissue and persistence of the disease following a subtotal thyroidectomy for exophthalmic goiter.[36] These and other mani-

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festations of the iodine reaction in exophthalmic goiter are of great interest, but the mechanism of their production will be understood only when the nature of the chemical changes in the thyroid is known.

RELATION BETWEEN THE PITUITARY AND THE THYROID [37]

Attempts to reproduce in man the effects that have been observed in animals during the administration of extracts of the anterior lobe of the pituitary have proved disappointing. Within the past six months we have had the good fortune to receive two extracts of the anterior lobe that produce an increase in metabolism in man. The extracts used were the growth hormone of E. R. Squibb & Sons and an extract of the anterior lobe manufactured under the name of Phyone by the Wilson Laboratories, Chicago.[38] We have administered these extracts subcutaneously to twenty-eight patients of various types. In eighteen of them the metabolism has shown an increase, which has always been temporary in spite of continued administration.

In ten of twelve patients who suffered from a moderate depression of the basal metabolism (minus 15 to minus 30 per cent) but whose clinical picture was not typical of hypothyroidism, the rate rose to normal or higher during the administration of the extract in association with clinical improvement. One of these patients has a pituitary tumor and another we believe to have Simmond's disease.

In two patients with marked myxedema no change was observed, although the extract was not given in sufficiently large doses to make this observation conclusive. In three patients with goiters and low basal metabolisms (minus 25 to minus 30 per cent) that we have attributed to an underfunction of the thyroid, the rate showed a well marked increase, and there was clinical improvement during administration of the extract. In one the goiter increased in size. In another the rate at which the basal metabolism dropped on omission of the extract was similar to the rate at which it drops from its point of maximum increase following a single large dose of thyroxine.

In three of six patients with normal basal metabolism and nontoxic goiters, and in one of four patients with normal basal metabolism but no goiter, the rate rose during the administration of the extract. In one of the patients with a nontoxic adenomatous goiter and a basal metabolism of minus 7 per cent the rate rose to plus 25 per cent in association with the development of tachycardia, weakness and increased sweating, clinical changes seen in mild cases of toxic adenoma.

In a patient with exophthalmic goiter, in association with an increase in basal metabolism from plus 28 per cent to plus 50 per cent there was marked increase in muscle weakness, nervousness, sweating and precordial pain, a slight increase in the prominence of the eyes and an increase in the size and firmness of the thyroid. During the injections a mild case of exophthalmic goiter became a moderately severe one. This observation must, of course, be confirmed in many other cases, but it coincides with the observations of Schockaert and Foster [39] and of Friedgood [40] in animals and naturally raises the question of the rôle of the pituitary in exophthalmic goiter.

SUMMARY

It has been calculated that in a normal man the thyroid forms thyroxine or its equivalent at the rate of about 0.3 mg. a day and that there are about from 10 to 14 mg. in the body outside of the thyroid gland.

Following the intravenous administration of a single dose of 10 mg. of thyroxine to a patient with myxedema, there is a marked lag in the clinical improvement behind changes in the metabolic rate, the period of highest metabolism being characterized by intoxication and the period of falling metabolism by improvement.

Observations on the calorigenic action of diiodotyrosine, thyronine, diiodothyronine and N-acetyl thyroxine show that the amino group, the diphenyl ether group and all four iodine atoms are essential for the maximum effect of thyroxine. Of special interest is the rather rapid return of the metabolism to the level before treatment following a single dose of diiodothyronine (from seven to eight days respectively in two patients with rates of minus 35 per cent and minus 40 per cent) compared with the slow return following a single dose of thyroxine (from seventy to eighty days at a level of minus 40 per cent).

The increase in metabolism produced by dinitrophenol in myxedema, with little or no clinical improvement, suggests that there may be different types of altered metabolism that cannot be differentiated by changes in the rate of oxidation alone.

As the complexity of the molecule of various thyroxine compounds increases, the greater will be their absorption from the gastro-intestinal tract and hence the less the effect of alkali in augmenting the absorption.

As a result of digestion with pepsin, data have been obtained which suggest that nearly all the calorigenic activity of the whole gland is possessed by less than half of the total iodine (acid-insoluble precipitate). The acid-soluble portion does possess slight calorigenic activity and after a single large dose the metabolism appears to return to its level before treatment more rapidly than after an equal change produced by the acid-insoluble precipitate. This finding has an important bearing on the United States Pharmacopeia method of standardizing desiccated thyroid by a determination of the total organic iodine.

After heating with approximately normal sodium hydroxide for four hours, desiccated thyroid loses more than two thirds of its calorigenic activity, whereas thyroxine is unaffected by the same treatment. This finding has an important bearing on the proposed standardization of desiccated thyroid by a determination of its thyroxine content.

The subcutaneous administration of extracts of the anterior lobe of the pituitary produced an increase in basal metabolism in eighteen of twenty-eight patients of various types, including two with hypopituitarism, ten with low basal metabolism of unknown cause, several with nontoxic goiters, including three patients with mild myxedema, and one case of exophthalmic goiter. During the injections in the patient with exophthalmic goiter, a mild case of the disease became a moderately severe one.

700 North Michigan Avenue.

37. Aided by a grant from the Squibb Foundation.

38. We are indebted to Drs. Anderson and Morrell and to Dr. Klein, respectively, for supplying these extracts.

39. Schockaert, J. A., and Foster, G. L.: Influence of Anterior Pituitary Substances on the Total Iodine Content of the Thyroid Gland in the Young Duck, J. Biol. Chem. **95**: 89 (Feb.) 1932.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. COLLIP AND ANDERSON, MEANS AND LERMAN, AND W. O. THOMPSON, PHEBE K. THOMPSON, TAYLOR, NADLER AND DICKIE

DR. GEORGE W. CRILE, Cleveland: We have listened to three very significant papers. The point I wish to make is that exophthalmic goiter is due to a pathologic physiology in the suprarenal-sympathetic system. If this is a fact, it is easy enough to put it to a test, and this my associates and I have done. In fourteen cases of typical primary hyperthyroidism and in twenty-four cases of recurrent hyperthyroidism, in each of which all the symptoms were present, we found that as the result of denervation of the suprarenal glands, without any operation at all on the thyroid gland, the disease as a whole disappeared. These results would suggest that the thyroid gland in and of itself is incapable of acquiring a hyperplasia or an excessive activity but that these are imposed on the thyroid gland most probably by the suprarenal-sympathetic system. A second interesting thing to me is a fact that bears on the pituitary. If it is a fact that division of the sympathetic system alone will completely arrest hyperthyroidism, these cases of basophilism of the pituitary should be controlled equally by denervation, because if the thyroid cannot acquire hyperplasia and develop exophthalmic goiter within itself or independently of the sympathetic nervous system I have a doubt whether the pituitary gland can acquire a basophilism by itself and independently of the sympathetic nervous system. We have tested this conception in a most interesting way. In one case presenting the whole symptom complex of polyglandular disease, denervation of the suprarenal glands cured the patient completely. All the symptoms disappeared. This would suggest that perhaps the possibility hasn't been sufficiently thought of that the sympathetic system itself governs the activity of all these glands, and that they, in turn, act on each other secondarily, just as the thyroid does on the body as a whole. Drs. Means and Lerman spoke about the resistance of certain patients to iodine. It is obvious that if compound solution of iodine should be given to a patient with neurocirculatory asthenia or any form of hyperkineticism not due to increased thyroxine, that patient would not be benefited. Furthermore, if a patient in whom neurocirculatory asthenia or some other form of pathologic stimulation of the suprarenal-sympathetic system was present, but whose symptoms in some degree were produced by an increased activity of the thyroid gland, then that patient's symptoms could not be entirely relieved by compound solution of iodine, because it is effective only against thyroxine, and, when thyroxine is not the sole cause of the disease, compound solution of iodine cannot offer complete relief.

DR. E. C. KENDALL, Rochester, Minn.: In regard to the important paper of Drs. Collip and Anderson, it will be of great interest to see whether they can produce an antihormone for all the rest of the hormones of the pituitary. It will be of still greater interest if they can produce an antihormone to insulin, to thyroxine, to the cortical hormone of the suprarenal, to epinephrine, and finally to cevitamic acid. If they do this, they are going to cause a great deal of trouble to present-day endocrinologists and clinicians and much more trouble to future medical students. I feel sure that the conclusions of Drs. Means and Lerman are in accordance with what is known of the effect of iodine. It certainly is not through its effect on the tissues; its effect is on the thyroid gland alone and is therefore variable under different conditions. The paper of Dr. Thompson and his co-workers was particularly interesting. Thyroxine was isolated twenty years ago this year. During the twenty years it has been found that there is no effect produced by desiccated thyroid that cannot be duplicated by pure crystalline thyroxine. I think it may safely be said that it is the sole active agent of the gland. I am inclined to believe that their conclusions concerning the acid insoluble fraction after enzyme action is best explained by small amounts of thyroxine that were not broken off by the enzyme action. When thyroxine is injected, a certain quantitative response is produced. If desiccated thyroid is administered, a certain quantitative response is produced. The response based on iodine in desiccated thyroid and iodine in thyroxine can therefore be compared. In all cases there is more effect from desiccated thyroid than would be expected from its thyroxine content. Analysis of desiccated thyroid shows that, on the average, 25 per cent of the total iodine is in the form of thyroxine; but the effect produced by the administration of desiccated thyroid indicates the presence of about four times this amount of thyroxine. This raises the question Is the thyroxine in desiccated thyroid more active than crystalline thyroxine because of an enhanced activity due to its peculiar form of combination within the protein or is there another explanation that is based on the fact that all of the crystalline thyroxine which is injected is not retained and utilized? I believe the simplest explanation is that only about 25 per cent of the crystalline thyroxine is retained in the body and held in the form that can function. The fact that the effect on the basal metabolic rate is in prbportion to the total iodine in desiccated thyroid and not to 25 per cent of the total iodine is a mere coincidence.

DR. HERRMANN L. BLUMGART, Boston: Drs. Collip and Anderson stated that increased activity of a hormone may be due, not to an increased amount or concentration of the hormone itself, but to a decrease in its antisubstance. Of interest in this connection are certain patients with the characteristic clinical features of thyrotoxicosis, the thyroid gland nevertheless appearing normal macroscopically and microscopically. I have observed two such patients this past year. Stricker reported a similar case in 1930 and other cases likewise have been observed. It is to be hoped that the work of Drs. Collip and Anderson may eventually make possible a lowering of thyroid activity in patients with chronic heart disease, making complete thyroidectomy unnecessary. Dr. Thompson and his co-workers referred to the differences in the metabolic actions of dinitrophenol and thyroid. My observations have been in accord with his. After removing the entire normal thyroid in patients with angina pectoris, feeding amounts of thyroid sufficient to bring the metabolic rate back to its preoperative level resulted in recurrence of attacks in five of six patients. Angina pectoris was precipitated after the same amount of effort that caused attacks before operation. When dinitrophenol was given instead of thyroid, the return to the preoperative metabolic level was not usually followed by a reappearance of angina. This, I believe, was due in large part to the fact that moderate metabolic rises after dinitrophenol do not entail a great increase in cardiac work. After dinitrophenol the increased oxygen is derived from each unit of blood, rather than, as in thyrotoxicosis, by an increase in the volume and velocity of blood flow. In using the term "basal metabolic rate" as an index of the amount of thyroid active principle within the body, one must recognize that other dissimilar agents may cause changes in the metabolic rate without necessarily influencing the work of the heart to the same degree. Measurements of the metabolic rate reflect only the calorigenic action of such substances. In the absence of dinitrophenol and certain unusual disease states, however, basal metabolic rate measurements still afford the best single index of either thyrotoxicosis with overactivity of the gland or of myxedema with underactivity of the gland.

DR. A. C. IVY, Chicago: The suggestion of Drs. Collip and Anderson that antihormones may be regarded as antibodies interests me because I have recently reported the experimental production of cretinism in rabbits by the injection of a thyrocytotoxic serum. This serum was prepared by injecting chickens with a saline extract of a rabbit's thyroid. Now having in mind their hypothesis concerning hormones and antihormones, I should like to ask how they would distinguish between a chalone and an antihormone. Until more is known about the nature of the material that Drs. Collip and Anderson are injecting and the nature of the reactions that they are obtaining, I do not warm up to the term "antihormone" and have the same criticisms concerning it that Dr. Kendall has pointed out. The point of this work, however, from a practical standpoint, is that when the physician injects an impure hormone product over a period of time he may observe an inhibitory or reversed reaction. Maybe the impurity in the product acts on the cells of the particular glands and destroys or inhibits them. Drs. Means and Lerman have expressed skepticism concerning the clinical existence of iod-Basedow disease. Experimentally, I believe that there is a basis for thinking that it may occur. I have in mind

the work of Webster and his co-workers in which they produced diffuse hyperplasia of the thyroid by feeding certain types of cabbage. Given this marked diffuse hyperplasia, the administration of iodine to these rabbits caused marked increase in basal metabolism, and if large doses of iodine were given the animals died. I think this to be a good indication that a certain state of the thyroid may occur in which the administration of iodine, particularly in large doses, may produce toxic effects. In the same connection, I should like to ask Drs. Means and Lerman this question, primarily for my own information: What happens to basal metabolism in those cases of colloid goiter in which, when iodine is given, a decrease in the size of the gland results? It is reported that in these cases histologic examination indicates that the colloid is thinned and then is absorbed from the acini into the blood. Theoretically, if the colloid in the gland is active the basal metabolic rate should go up, at least occasionally. The papers of Drs. Means and Lerman and of Dr. Thompson and his co-workers clear up a number of points in regard to the rôle of iodine in exophthalmic goiter, but the mechanism of "refractoriness to iodine" and some of the apparent paradoxical effects of iodine on the thyroid remain to be elucidated. Some physiologists used to say that the action of thyroid extract is due primarily to its stimulating action on metabolism and that if some other substance would stimulate metabolism to the same extent that thyroid extract does, this substance would have the same effects on the body that thyroid extract does. The work that has been done by Dr. Thompson and others with dinitrophenol renders such a statement no longer tenable. That is, thyroid extract has specific effects on the body other than raising the metabolic rate.

DR. GEORGE M. CURTIS, Columbus, Ohio: In the work presented, the main evaluation of thyroid function has been based on the basal metabolic rate. My studies indicate that two other factors are as important, perhaps more so, in judging thyroid activity. I refer to the blood iodine and the urinary excretion of iodine. During the past ten years, and particularly since the work of von Fellenberg and his pupils Sturm and Lunde, considerable information has become available concerning the blood iodine and the daily loss of iodine in the urine. The blood iodine is an index of thyroid function. Following total thyroidectomy for cardiovascular disease, the blood iodine decreases to one-third its normal level. The two-third decrease corresponds to the alcohol insoluble fraction, which has been designated "organic" and which presumably contains the thyroid hormone. The loss of sugar in the urine is significant in evaluating the activity of the pancreatic islets. The loss of calcium in the urine is significant in evaluating parathyroid function. In the same manner the daily loss of iodine in the urine becomes of significance in evaluating thyroid activity. The thyroid hormone, as thyroxine or in whatever form it exists in the circulating blood, has a high iodine content. I have found an increased loss of iodine in the urine in patients with hyperthyroidism. The investigation of Drs. Collip and Anderson has raised a new point of view concerning thyroid function, and particularly regarding the extrathyrogenic factor of exophthalmic goiter. I would suggest three methods of determining the resultant changes in thyroid function: the basal metabolic rate, the blood iodine and the daily urinary loss of iodine. Drs. Means and Lerman "doubt but do not deny" the existence of "iod-Basedow," that is, of iodine induced hyperthyroidism. This is in accord with my experience. It is not possible to produce readily "iod-Basedow." I have seen the blood iodine rise from 12 to more than 7,000 micrograms per hundred cubic centimeters subsequent to high iodine administration, without any evidence of hyperthyroidism. This is the common experience. There would appear to be an iodine deficiency factor in the genesis of hyperthyroidism. It is difficult to harmonize this with refractoriness to iodine. Further investigation is necessary. The demonstration of Dr. Thompson and his co-workers of other than thyroxine iodine in the thyroid gland is in accord with my studies. I have even gone so far as to inquire whether iodine has another function in the human body, outside of the formation of the high iodine containing thyroid hormone.

DR. HAROLD T. HYMAN, New York: I would like to corroborate what Drs. Means and Lerman have said about the therapeutics of iodides in the treatment of the diseases of the thyroid gland. In 1920, with my late colleague Dr. Kessel, I demonstrated the spontaneous course of exophthalmic goiter, showing that it was subject to exacerbations and remissions. It was our belief that the effect of the iodides would vary depending on whether the patient was treated in an up-hill phase of the disease or whether the patient was in a remission. Obviously the iodide effects would be more dramatic if the patient was seen during a remission. Obviously, too, if the patient received iodides during the exacerbation of the disease or an up-hill phase the amount of iodide effect might not be sufficient to overcome whatever it is that is the fundamental pathogenic factor in exophthalmic goiter. In consequence of this, one may have the spectacle of a therapeutic measure that is of value with the patient actually being worse for the time being. Under such circumstances the iodide should not be stopped but should be persisted in and the dosage increased. In a few instances in which patients were brought to us desperately ill with thyrotoxic storms, we had the temerity to treat them with thyroxine, and in a few instances we thought we observed a genuinely specific effect. That point of view has been unpopular and has not been accepted even by our colleagues in our own institution, and for many years we have begged them to show us iod-Basedow when it appeared. Our experiences have been that the patients who had exacerbations of their disease when iodides were administered were either those who were caught in an up-hill phase or those in whom some extraneous factor was operating. I remember a woman who became very much worse while on iodide, and we discovered that the increase in her symptoms and her basal metabolic rate was due to the fact that next bed to her a patient was admitted with pneumonia. When her bed was moved to another corner of the room, her basal metabolic rate fell. The importance of these observations cannot be overemphasized, because the majority of clinicians have been frightened about the use of iodine. In the first place, they were frightened because of the dictum that with adenomatous thyroid the iodide was of less value than in true hyperthyroidism. Then they were frightened into the belief that in simple goiter, true exophthalmic goiter might be produced by iodide administration. All of these fears should be put to rest permanently. The contribution of Drs. Means and Lerman will be a great step forward in the intelligent use of iodides by the general practitioner.

DR. D. ROY MCCULLAGH, Cleveland: Dr. Crile has suggested that on account of the research on iodine which we have been doing in the biochemical department at the Cleveland Clinic, I might wish to comment on some of the papers. Most of the remarks that I would have attempted to make have already been made. As Dr. Curtis has said, the test for blood iodine is now relatively simple and accurate and is unquestionably of valuable diagnostic assistance. I think, however, that Dr. Curtis will agree that frequently the blood iodine, although elevated, does not seem to be as high as one would expect, as indicated by the general symptoms. This ultimately may have some important bearing on the explanation of the nature of exophthalmic goiter. I think possibly there may be substances other than thyroxine which alter metabolism in that condition. I should like to comment also on the startling reports from the group at Montreal. The natural thought, as Dr. Ivy has mentioned, is that the observations reported by Drs. Collip and Anderson might be due to immunologic phenomena. Certain observations have been reported elsewhere by Dr. Collip that lead one to question this assumption. The final proof of whether or not there are real physiologic antihormones will be the isolation of these substances from normal animals or persons that have not been injected with hormone. The latter has already been reported and furnishes suggestive evidence that the antihormone theory is tenable. Our work at the clinic in collaboration with Dr. Walsh is also suggestive. Working with the testicular hormone, we were unable to replace completely the functions of the testes when injecting this hormone. For this reason, we felt that there was a possibility that there was some other active internal secretion, and our work led us to postulate the existence of a chalone in the testes which apparently has the property of decreasing the size of the prostate; that is, the opposite property of the recognized testicular hormone. This, if true, would be an example, and a truly physiologic example, of the conception that Drs. Collip and Anderson have presented.

DR. WALTER M. BOOTHBY, Rochester, Minn.: I agree with Drs. Means and Lerman that, so far as is known, no patient with exophthalmic goiter has ever been made worse by the proper use of iodine. The aggravation of the symptoms that frequently occurs when iodine is stopped or used intermittently must be differentiated and these patients cannot be considered as being made worse by its use. The use of iodine as a test for exophthalmic goiter has its limitations as well as its advantages and requires an accurate knowledge of the normal course of the disease as well as a thorough understanding of the effect of iodine. A fact usually not recognized is important in this connection; namely, the beneficial effect of iodine does not usually appear until ten days or two weeks after its administration has been started, and the beneficial effect thus produced lasts usually about the same length of time; the intermittent administration of iodine is bad and when used is frequently based on alternate weeks or alternate two weeks and therefore the effect of its action can easily be misinterpreted. Drs. Means and Lerman say that they believe there is no such thing as "iod-Basedow." If the term is used to indicate that true Basedow's disease (true Grave's disease, true exophthalmic goiter), then their statement is correct. However, there is some evidence in this country and more evidence in the endemic goitrous districts of Europe that a certain number of patients with endemic goiter are rendered hyperthyroid by the administration of iodine. Plummer has always insisted that the hyperthyroidism of adenomatous goiter is a separate clinical entity and should be chiefly differentiated from true exophthalmic goiter —the failure to do so has prevented the earlier recognition of when iodine is and is not beneficial in the treatment of various thyroid conditions.

DR. J. B. COLLIP, Montreal: I do not think it is the time and place to enter into a defense of the theory that we have suggested. We have presented certain facts which we feel will stand the test of further investigation, but our theoretical presentation may be wrong, it may be partially true or it may all be true. We were interested in this theory primarily as a basis for directing our own future work. Already, as Dr. McCullagh has said, we have suggested evidence supporting certain phases of the theory. In regard to the use of the word "chalone," I do not think that the point of view which we have presented in our theoretical discussion is such that it is right to use the word "chalone" for the group of substances we are calling antihormones for lack of a better word. The terminology is in rather a bad shape, it is true. One may question rightly the use of the word "hormone" at all. A hormone, as it was thought of years ago, is supposed to act on the body as a whole. All of these pituitary principles which we have been dealing with lately act on another organ and there is, as Dr. Kendall has pointed out in private discussion, a real point of difference between this group of pituitary principles and other hormones. I was interested in the remarks of Dr. Curtis with regard to the possible use of iodine values of blood and urine as indicating the state of thyroid functioning; Dr. McCullagh has now available a method that will make it quite simple apparently for a number of workers to apply this method.

DR. J. H. MEANS, Boston: I doubted the existence of iod-Basedow; I don't deny its existence, but I have never seen it. What Dr. Boothby says is important. The endemic in Switzerland is much more intense than anything known in this country. That may be the explanation. However, I was interested in Bern last summer to talk to Professor Dautrebande of Liége. He told me he also thought there was no such thing as iod-Basedow, in the sense the term is used today; namely, thyrotoxicosis produced by the giving of iodine. He said the cases he had seen, that had been called by his European brethren iod-Basedow, in his hands had responded to iodine therapy just like other cases of thyrotoxicosis. I am very grateful to Dr. Curtis. I think his work is of extraordinary importance, and in following lines of the sort that he is lies the solution of some of these complicated problems about the thyroid. I was asked a question by Dr. Ivy. I can't answer it. I haven't the faintest idea how colloid gets out of the thyroid. I have seen colloid being put into the follicles but I have been unable to discover that anybody knows how it gets out. I don't even know whether it gets out, when iodine is given in colloid goiter. Of course, we have very little endemic goiter in Boston, so that I am not an authority on colloid goiter. But it does occur to me that if there is a reduction in size, and generally we don't get any reduction when we give iodine to people with sporadic colloid goiter, it may be because of differences in vascular engorgement. I didn't quite follow Dr. Ivy's comment on the nature of the calorigenic action of thyroxine in relation to dinitrophenol. I think they are totally different. I think thyroxine has a calorigenic action, and a whole lot of other actions, which dinitrophenol does not possess, and that the effect of thyroxine on the body is peculiar to thyroxine and can be imitated by nothing else that is available today.

DR. W. O. THOMPSON, Chicago: With regard to the acid-soluble fraction which Dr. Kendall said probably depended for its activity on thyroxine, I want to point out that we have not said what its activity depends on because we do not know. Dr. Kendall has suggested that the discrepancy between the effect of thyroxine and desiccated thyroid may be more apparent than real because of relatively greater utilization of desiccated thyroid. He has wisely pointed out that one of the chief criticisms of our work is that we do not know how much of the active principles of the various substances administered was excreted unused. Nevertheless, I think that it has not yet been definitely proved that desiccated thyroid is utilized better than thyroxine, and in different patients the same dose of desiccated thyroid may produce very different effects. It is difficult to see how greater utilization of desiccated thyroid than of thyroxine would explain the great reduction in the calorigenic activity of the former as a result of heating with alkali.

MENINGOCOCCIC MENINGITIS

A NEW FORM OF THERAPY

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Weischselbaum,[1] although not credited with priority [2] in observing the meningococcus, isolated and cultured it in 1887; thus he laid the foundation for the present etiologic conception of the disease. Jochmann [3] initiated the clinical intrathecal use of an antiserum evaluated earlier by animal experimentation by Kolle and Wassermann.[4]

Flexner in 1907-1908 [5] reviewed the entire subject of meningococcic meningitis and as the result of extensive laboratory and clinical investigations demonstrated the value of an antimeningitis serum in the treatment of the disease. He attributed the benefits of the serum clinically to its antibacterial qualities.

This work has stood unquestioned, and very little change has been made in methods of preparation of serums, largely because the ability of the meningococcus to elaborate a toxin was not recognized. None of the more important articles on the subject, including the comprehensive reviews of Gordon [6] in 1920 and Murray [7] in 1929, admit the possibilities of the production of a

1. Weischselbaum, A.: Ueber die Aetiologie der akuten Meningitis cerebro-spinalis, Fortschr. d. Med. **5**: 573, 1887.
2. Cited by Park, W. H., and Williams, Anna W.: Pathogenic Microörganisms, Philadelphia, Lea & Febiger, 1933, p. 371.
3. Jochmann, G.: Versuche zur Serodiagnostik und Serotherapie der epidemischen Genickstarre, Deutsche med. Wchnschr. **32**: 788, 1906.
4. Kolle, Wilhelm, and Wassermann, August: Versuche zur Gewinnung und Wertbestimmung eines Meningococcenserums, Deutsche med. Wchnschr. **32**: 609, 1906.
5. Flexner, Simon: Experimental Cerebrospinal Meningitis in Monkeys, J. Exper. Med. **9**: 142, 1907; Concerning a Serum Therapy for Experimental Infection with Diplococcus Intracellularis, ibid., p. 168. Flexner, Simon, and Jobling, J. W.: Serum Treatment of Epidemic Cerebro-Spinal Meningitis, ibid. **10**: 141, 1908: An Analysis of Four Hundred Cases of Epidemic Meningitis Treated with the Anti-Meningitis Serum, ibid., p. 690.
6. Gordon, M. H.: Cerebrospinal Fever, Medical Research Council, special report series, No. 50, 1920.
7. Murray, E. G. D.: The Meningococcus, Medical Research Council, special report series, No. 124, 1929.

soluble toxin but do agree to the elaboration of an endotoxin. Murray [7] states that "no one has yet succeeded in demonstrating a soluble toxin in meningococcus cultures and all are ready to admit that such a toxin is not produced."

Efforts to associate any one type of the meningococcus or any particular strain with various epidemics have not been successful.[8] Clinicians generally agree that the present polyvalent antibacterial serums and methods of standardization are not wholly satisfactory, and this was well demonstrated in 1929 by Wright,[9] who showed in an outbreak observed by him that "a serum uniformly of the highest titer was not effective clinically." I have made somewhat similar observations in the contagious disease department of the Cook County Hospital.

TABLE 1.—*Reasons for Discarding Cases from Report*

Reason	Number of Cases
Received both antitoxin and antiserum	16
Questionable diagnosis	17
No serum given	7
Incorrect diagnosis reported	11
Miscellaneous	20
Records absent from file	5
Total	76

In an attempt to clarify the perplexities of the situation in regard to antimeningococcus serum, Ferry [10] recently succeeded in demonstrating soluble exotoxins in bouillon filtrates of the four recognized Gordon types of the meningococcus. These toxins, when injected individually into animals, developed specific antitoxins. Convalescent serums were shown to possess neutralizing properties toward homologous soluble toxins. Less extensive, but corroborative, work on the toxin [11] and antitoxin [12] has been recorded.

Ferry concludes from his observations that the symptoms of meningococcic meningitis in laboratory animals (guinea-pig [12a] monkey [13] and rabbit [14]) result from a selective action of the toxin toward the cerebrospinal nervous system. He found that animals receiving lethal doses of toxin intracisternally or lethal doses of viable culture intraspinally could be protected by intraperitoneal injections of antitoxin [12b] but not by standard antimeningococcus serum,[12c] and that animals immunized by sublethal intracisternal doses of toxin were resistant to lethal doses of live culture. Ferry [15] reports elsewhere in this issue that susceptible human beings can be immunized against meningococcus toxin as revealed by subsequent skin test.

The experimental antitoxin [16] used in the present clinical study was of the same lots reported on by Ferry.[17] This antitoxin was prepared by injecting horses subcutaneously with increasing doses of the individual soluble toxins of the four types of meningococci.[10] The antitoxin property of the serum was determined by its ability to neutralize toxin, as shown by intradermal injection in susceptible human beings and by its ability to protect laboratory animals from lethal doses of toxin and culture. Concentrated antitoxin was used in a few of the cases in my series. This was prepared by standard concentration methods.

Three hundred and seventy-two patients [18] were discharged from the Cook County Hospital, Contagious Disease Department, from November 1932 to June 1934, with the diagnosis "epidemic meningitis." Of these, the records of 296 have been included in this report, the remaining being discarded for various reasons (table 1).

The 296 patients have been separated into a series of eighty-five receiving meningococcus antitoxin and a series of 211 receiving two well known standard brands of antimeningococcus serum. The clinical diagnosis of all but forty cases was verified by smear or cultural identification of the specific micro-organism in the spinal fluid.

Approximately every fifth to seventh patient received the experimental antitoxin during the early studies and every third patient during the latter half of the period. Patients to receive the antitoxin were selected only by reason of their not having had previous antimeningococcus serum therapy. It was the general impression among the hospital personnel that the patients treated with antitoxin were as a group more severely ill and had less hopeful prognosis on admission than those treated with the standard serums. This was undoubtedly true during the latter half of the period as the efficacy of the antitoxin became more apparent. The resident staff was specifically instructed not to withhold antitoxin when an untreated case presented itself, regardless of the prognosis. All fatalities have been analyzed on the basis of their relation to the date and hour of admission without reference to complications or instances of delayed treatment. All antitoxin deaths that occurred are classed as therapeutic failures and any factor that might show a lower and more favorable death rate for the antitoxin series has been studiously avoided. The patients in many instances were police patrol pickups without family or friends; on several

TABLE 2.—*Comparison of Fatality Rates of Cases of Meningococcic Meningitis in Which Meningococcus Antitoxin and Standard Antimeningococcic Serum Were Given*

Therapy	Number of Cases	All Deaths	Excluding Cases Fatal Within		
			24 Hours	36 Hours	48 Hours
Antitoxin	85	23.5%	17.5%	10.9%	9.6%
Antiserum	211	45.9%	40.9%	35.9%	29.6%
All cases	296	39.5%	34.2%	28.6%	22.6%

8. Wadsworth, A.: Meningococcus Meningitis: The Results of Recent Investigation in Relation to Serum Therapy, Am. J. Hyg. **14**: 630 (Nov.) 1931.

9. Wright, I. S.; De Sanctis, A. G., and Sheplar, Adele: The Determination of the Value of Serum in the Treatment for Meningococcus Meningitis, Am. J. Dis. Child. **38**: 730 (Oct.) 1929.

10. Ferry, N. S.; Norton, J. F., and Steele, A. H.: Studies of the Properties of Bouillon Filtrates of the Meningococcus: Production of a Soluble Toxin, J. Immunol. **21**: 293 (Oct.) 1931.

11. Sédallian, P., and Naussac, H.: Recherches sur la toxine méningococcique, Compt. rend. Soc. de biol. **111**: 393 (Oct. 28) 1932. Branham, S. E., and Lillie, R. D.: Experimental Meningitis in Guinea-Pigs, J. Bact. **25**: 90 (Jan.) 1933. Sickles, Grace M.: The Standardization of Antimeningococcus Serum: The Titration of Its Neutralizing Potency by the Phenomenon of Local Skin Reactivity, Am. J. Hyg. **17**: 412 (March) 1933. Krestownikowa, W.; Belkina, A.; Dosser, E., and Lasowsky, I.: Ueber das Meningokokkentoxin, Ztschr. f. Immunitätsforsch. u. exper. Therap. **78**: 451, 1933.

12. (*a*) Ferry, N. S.: Meningococcus Antitoxin: I. Prophylactic and Therapeutic Tests on Guinea-Pigs, J. Immunol. **23**: 315 (Oct.) 1932; (*b*) II. Therapeutic Tests on Monkeys, ibid., p. 325; Meningococcus Toxin and Antitoxin: III. Further Tests on Monkeys, ibid. **26**: 133 (Feb.) 1934.

13. Ferry (references 12*b* and 12*c*).

14. Ferry, N. S., and Schornack, P. J.: Meningococcus Toxin and Antitoxin: IV. Further Tests on Guinea-Pigs and Rabbits, J. Immunol. **26**: 143 (Feb.) 1934.

15. Ferry, N. S., and Steele, A. H.: Active Immunization with Meningococcus Toxin, this issue, p. 983.

16. Meningococcus antitoxin prepared by Dr. N. S. Ferry was supplied through the courtesy of Parke, Davis & Co., Detroit.

17. Ferry.[12] Ferry and Schornack.[14]

18. I am indebted to other members of the Contagious Disease Hospital Staff (Cook County) for permission to treat patients assigned to their service while conducting this study, and to the resident staff and the nursing service for their helpful cooperation.

occasions, identification could not be established prior to death or convalescence. Very frequently adequate history could not be elicited and therefore statistical figures for cases entering this hospital cannot be compared with other institutions in the city.

The fatality rate for the combined series is 39.5 per cent, with 53 per cent of the deaths occurring within forty-eight hours after hospital admission. The efficacy

TABLE 3.—*Cases and Deaths by Ten-Year Age Groups*

Age Group	Cases	Deaths	Fatality Rate
1 to 10	89	18	20.2%
11 to 20	69	23	33.3%
21 to 30	51	15	29.4%
31 to 40	34	18	52.9%
41 to 50	22	16	72.7%
51 to 60	14	12	85.7%
61 to 70	4	4	100.0%
71 to 80	4	4	100.0%
Unknown	9	7	77.7%

of the antitoxin over antimeningococcus serum is apparent by comparison of the respective fatality rates of treated cases occurring at the same time, in the same hospital and under the same supervision. Consequently seasonal variations that might influence virulence of the meningococci are eliminated from the contrasted figures of table 1. Twenty deaths occurred in the series of eighty-five patients treated with meningococcus antitoxin; 117 deaths were recorded in the group of 211 patients treated with antimeningococcus serum. The percentage death rate was 23.5 for the antitoxin and 45.9 for the antiserum.

The age of patients included in the entire series ranged from 3 months to 80 years, averaging 22.7 years. The cases treated with antitoxin averaged 18.1 years and the antiserum-treated group 24.7 years. From a study of table 3, arranged in ten-year age groups and respective fatality rates, it appears that the antitoxin was given to the most favorable subjects.

Seventy-three antitoxin treated patients and 138 antiserum treated patients were 30 years of age or younger. These cases are arranged in ten-year age groups in table 4 and show that, regardless of age, the antitoxin resulted in a lower fatality rate. Above the age of 30 the ratio is more favorable, but the number of antitoxin treated cases is not sufficient to warrant comparison.

TABLE 4.—*Influence of Age on Antitoxin and Antiserum Therapy*

Age	Cases		Deaths		Fatality Rates	
	Antitoxin	Antiserum	Antitoxin	Antiserum	Antitoxin	Antiserum
1 to 10	32	56	4	15	12.5%	26.7%
11 to 20	22	48	6	17	27.2%	35.4%
21 to 30	19	34	2	13	10.5%	38.2%
Totals	73	138	12	45	16.4%	32.6%

The period of hospitalization for all recovered patients averaged 17.3 days. It is notable that those receiving antitoxin averaged 16.2 days as compared to the antiserum treated group, which averaged 18.0 days per case. The average hospitalization time for 338 cases at the Cook County Hospital recently reported by Borovsky [19] was twenty-three days.

Table 5 shows the cases discharged from Cook County Hospital diagnosed "epidemic meningitis," 1915-1933 inclusive, with respective fatality rates. An improvement in the fatality rate during 1933 over other comparable years is seen. During 1933 in approximately 20 per cent of the cases reported the patients received antitoxin, and its effect on the death rate for that year is significant.

The average total amounts of experimental antitoxin and standard serum given to a patient who had recovered was approximately 161.7 cc. and 123.5 cc. respectively. The largest amount of antitoxin and standard serum administered in recovered patients was 360 cc. for the former and 245 cc. for the latter, and the smallest amount 75 and 40 cc. respectively. Allergic manifestations occurred in 17.7 per cent of the antitoxin treated cases as compared to 28.9 per cent of those in which standard serum was given. In no instance did an ocular or auditory complication develop after the institution of antitoxin therapy; nevertheless, large doses of antitoxin were sometimes given in unsuccessful efforts to overcome such conditions when present at the time of the patient's admission.

Of eighty-five patients receiving the antitoxin, cisternal puncture was resorted to on only five occasions

TABLE 5.—*Epidemic Meningitis: Annual Reports of Librarian, Cook County Hospital, Chicago*

Year	Cases	Deaths	Fatality Rates
1915	24	16	66.6%
1916	21	14	66.6%
1917	178	92	51.7%
1918	145	69	47.5%
1919	49	20	40.8%
1920	21	19	90.4%
1921	20	10	50.0%
1922	9	6	66.6%
1923	20	7	35.0%
1924	44	36	81.7%
1925	5	0	0.0%
1926	13	9	69.2%
1927	83	48	57.8%
1928	187	85	43.3%
1929	235	136	57.8%
1930	134	73	54.4%
1931	224	112	50.0%
1932	116	56	48.2%
1933	287	111	38.7%
Total	1,815	919	50.6%

on as many patients. In only three instances and on the same number of patients were spinal drainage and treatment done twice during the same calendar day. The average number of lumbar punctures per case was not materially reduced except in a group of patients receiving antitoxin intravenously and intramuscularly.

In twenty-eight extremely severe but uncomplicated cases, 20 cc. or more of meningococcus antitoxin was given intravenously or intramuscularly; of these patients eight died, with a fatality rate of 28.6 per cent. The twenty patients who recovered received an average of 173.6 cc. of antitoxin per patient, of which an average of 58.5 cc. was given intravenously and/or intramuscularly and 115.1 cc. per patient intraspinally. The period of hospitalization for this group averaged 13.6 days per case as compared to 17.5 days for the combined series.

SUMMARY

My experiences during the past one and one-half years seem to justify certain conclusions regarding the treatment of meningococcic meningitis. Meningococcus antitoxin has reduced by approximately 50 per cent the deaths from meningococcic meningitis at Cook County Hospital.

For many years it has been customary in the Contagious Disease Department of the Cook County

19. Borovsky, M. P. Clinical Study of Meningococcus Meningitis, Illinois M. J. **64**: 532 (Dec.) 1933.

Hospital to administer antimeningococcus serum intrathecally not oftener than once in twenty-four hours. This plan was adhered to when meningococcus antitoxin was given. Lumbar punctures when made every twelve hours or at eight hour intervals, as sometimes recommended, are extremely disturbing to many patients and seem to be of no added value in lowering the fatality rate.

Although cisternal punctures are much more easily performed by one with experience than lumbar punctures and are often preferred by the patient, this procedure should not be encouraged in a public hospital in which interns and residents are frequently changed. I do not believe that cisternal puncture is necessary in the treatment of meningococcic meningitis in order to secure the most efficient results. It is not essential to adopt this route for the purpose either of drainage or of administration of serum except in case of block in the spinal canal. In no instance among the entire series of 372 patients was an intraventricular puncture required.

In the brief report [20] of a meningococcic meningitis patient treated at Cook County Hospital in 1918, the value of giving antimeningococcus serum intravenously was emphasized. Since that time it has been customary to resort to intravenous serum therapy for all adult meningococcic meningitis patients admitted to my service. The value of this procedure is still more apparent when antitoxin instead of antimeningococcus serum is the remedy. As our experience with the antitoxin increased, larger and larger amounts of meningococcus antitoxin were given intravenously. The dose ranged from 20 cc. among the earlier cases up to 100 cc. and more during recent months. These large amounts of antitoxin intravenously explain chiefly the greater average dose of antitoxin as compared with antimeningococcus serum. On the other hand, the greater the quantity of antitoxin given intravenously, the smaller the average amount required for intrathecal injection. The most outstanding feature of intravenous and intramuscular antitoxin treatment is the prompt response of the infection and a more than 20 per cent reduction in the period of hospitalization. In fact, it is my impression that eventually it may be regarded as entirely unnecessary to administer any serum intrathecally if sufficient antitoxin is injected intravenously. Under such circumstances lumbar puncture would be done only for the purpose of diagnosis and for drainage.

A problem is now under way to compare the efficacy of intravenous and intramuscular methods of administration supplementing intrathecal antitoxin. One young woman with a fulminating type of meningococcemia whose child died of meningococcic meningitis was treated only by large doses of antitoxin intravenously. Meningeal infection did not progress and she was discharged completely recovered on the seventh hospital day.

For the treatment of meningococcic meningitis with meningococcus antitoxin the following plan may be followed:

1. Intravenously from 60 to 100 cc. of the antitoxin is administered in from 120 to 200 cc. or more, respectively, of physiologic solution of sodium chloride or 10 per cent dextrose solution. The smaller amount may suffice for a child, the larger quantity for an adult. This form of treatment may be repeated daily if the condition of the patient seems to require it. As a rule, one large dose intravenously when therapy is started will prove sufficient by this route.

2. Intraspinally the amount of antitoxin, undiluted, and given by the gravity method, will be governed by the volume of spinal fluid withdrawn. Usually the quantity of antitoxin administered should be less than the amount of spinal fluid released. The initial dose of antitoxin intraspinally will usually vary from 20 to 40 cc. Daily punctures should be made until the fluid is clear and free from organisms. At such a time the cell count of the spinal fluid will generally be less than 100.

3. Intramuscular administration of serum in an initial dose of from 30 to 60 cc. is of value, but because of the serious nature of the disease the intravenous route is to be preferred.[21]

25 East Washington Street.

20. Hoyne, A. L.; Arkin, H. S., and Sherman, M. J.: Treatment of a Severe Case of Epidemic Meningitis by Combined Intravenous and Intraspinal Injections of Antimeningococcus Serum, J. A. M. A. **72**: 22 (Jan. 4) 1919.

ACTIVE IMMUNIZATION WITH MENINGOCOCCUS TOXIN

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In 1931 it was shown [1] that bouillon filtrates of young cultures of the four recognized Gordon types of the meningococcus contain soluble or extracellular toxins specific to the individual types, as well as a toxin common to all types, and that animals injected with these toxins develop antitoxins specific to their homologous toxins and an antitoxin more or less common to all types (a clinical study of this antitoxin will be found elsewhere in this issue of THE JOURNAL [2]).

It was also shown that a certain proportion (about 50 per cent) of children are susceptible to one or more of these toxins, following intracutaneous injections of the diluted toxin, the test being carried out in a manner similar to the Schick and Dick tests for susceptibility to diphtheria and scarlet fever, respectively.

It was later demonstrated [3] that this soluble toxin has a specific action on the central nervous system of laboratory animals, especially the monkey, and that when injected intracisternally it produces symptoms similar in nature and approaching in severity those

21. Since the preparation of this paper, twenty-three additional patients with meningococcic meningitis have been treated in the contagious disease department of the Cook County Hospital. Six of this number received standard makes of antimeningococcus serum. The other seventeen were treated with the experimental meningococcus antitoxin. In the first group, three of the six who received the standard antimeningococcus serum died. The youngest of the three who died was 7 months old and the eldest 5½ years. Of the three who recovered, one was treated with the experimental antitoxin after he failed to respond to the standard serum. In the antitoxin group of seventeen there was but one death—that of a man, aged 38, with a history of alcoholism, who died the third day after admission. Of the remaining sixteen who recovered, the youngest was 5 months of age and the eldest 35 years. By adding the seventeen antitoxin cases mentioned here to the eighty-five previously analyzed it is found that of the 102 patients with meningococcic meningitis who were treated with experimental antitoxin there were twenty-one deaths, or a fatality rate for the entire series of 20.5 per cent.

From the Research Laboratories, Parke, Davis and Company, Detroit, and the Wayne County Training School, Northville, Mich.

1. Ferry, N. S.; Norton, J. F., and Steele, A. H.: Studies of the Properties of Bouillon Filtrates of the Meningococcus: Production of a Soluble Toxin, J. Immunol. **21**: 293 (Oct.) 1931.

2. Hoyne, A. L.: Meningococcus Meningitis: A New Form of Therapy, this issue, p. 980.

3. Ferry, N. S.: Meningococcus Toxin and Antitoxin: III. Further Tests on Monkeys, J. Immunol. **26**: 133 (Feb.) 1934. Ferry, N. S., and Schornack, P. J.: Meningococcus Toxin and Antitoxin: IV. Further Tests on Guinea-Pigs and Rabbits, ibid., p. 143.

resulting from intraspinal inoculations of live meningococci. It was discovered at that time that recovery from previous intracisternal injections of the toxin induced a state of active immunity in those animals against an intraspinal inoculation of a fatal dose of live organisms, similar to that immunity, following recovery from the disease, shown previously in one of these studies.[4]

The meningococcus, therefore, produces a true soluble toxin that will stimulate an active immunity in laboratory animals against the live organism as well as its toxin.

The present work was carried out to determine whether active immunity against the toxin, or at least the skin test dose of toxin, could be induced in man by a series of subcutaneous injections of the undiluted toxin. Accordingly, a large number of children, ranging from 12 to 18 years of age, were skin tested and those showing positive reactions to one skin test dose of the toxin were injected subcutaneously with the undiluted material.[5]

The method of procedure was as follows: A toxin was prepared from type I-III culture of the meningococcus and diluted according to a standard toxin, so that 0.1 cc. contained a skin test dose. This dose was previously determined to be that amount of toxin which, when injected intracutaneously in a dose of 0.1 cc. into an individual susceptible to the toxin, will produce a local skin reaction at least 10 mm. in diameter. The diagnostic test toxin used in this work contained 5,000 skin test doses per cubic centimeter. All individuals were injected intracutaneously with 0.1 cc. of this test toxin. Those showing a skin reaction of 10 mm. or over in diameter were considered susceptible and were later injected with the immunizing toxin. Since it was believed that skin tests with one toxin should be sufficient to demonstrate the point in question, the children were not subjected to tests with toxins of all four types. The immunizing toxin, on the other hand, was composed of an equal mixture of toxins of the four types and contained, in all, 5,000 skin test doses per cubic centimeter, approximately 1,250 skin test doses in each of the four toxins. The susceptible children to be immunized were divided into two groups. One group was given three injections of the following doses of the mixed toxin one week apart: 0.1 cc., 0.5 cc., and 1 cc., equivalent to 8,000 skin test doses in all. The other group was given four injections, also one week apart, the doses being 0.1 cc., 0.5 cc., 1 cc. and 1.5 cc., equivalent to 13,500 skin test doses. As the immunizing toxin contained approximately an equal amount of each individual toxin, it is evident that the toxin homologous to the test material represented but from one fourth to one third of the whole, depending on the amount of toxin common to all types present in the mixture. In other words, the children injected with the four doses did not receive more than the equivalent of 4,000 skin test doses of any one of the type toxins.

Results

Number tested	605	
Number positive	285	47.1%
Number injected	232	
Three Dose Group—Number in Group 149		
Negative reactors on retest	93	62.4%
Reactions smaller than original	38	25.5%
Reactions same size as original	11	7.3%
Reactions larger than original	7	4.7%
Four Dose Group—Number in Group 83		
Negative reactors on retest	62	74.6%
Reactions smaller than original	7	8.4%
Reactions same size as original	7	8.4%
Reactions larger than original	5	6.0%
Reactions very large	2	2.4%

At the end of eight weeks all children were retested with a skin test dose of toxin to determine the number of those who had become immune to the toxin.

Three types of reaction to the injection of undiluted toxin were observed. First, local reactions: About 50 per cent of the children showed local reactions mostly of a mild character, which caused the child to complain only of slight soreness or stiffness of the arm. Second, general or systemic reactions: Approximately 10 per cent of the group exhibited mild systemic reactions, following the second or third injection, the symptoms of which were headache, dizziness, gastro-intestinal upsets and a slight elevation of temperature. These reactions invariably disappeared within eighteen hours. Third, allergic reactions: In four instances immediate reactions after the second injection, consisting of generalized urticaria and, in one case, abdominal cramps accompanied by mild prostration. These symptoms were promptly controlled by an adequate dose of epinephrine. Further injections were discontinued in these cases as a precautionary measure.

Out of the 285 positive reactors fifty-three, for one reason or another, did not receive full treatment and were not retested.

Of the 232 who were given the full number of injections and were retested, including both groups, 155, or 66.8 per cent, gave negative reactions on retesting. Had the amount of toxin been increased, or had only the homologous toxin been given, the percentage of negative reactors would undoubtedly have been higher.

COMMENT

This work has demonstrated two facts: first, that certain individuals who are susceptible to the skin test dose of meningococcus toxin can be made immune to this dose of toxin by at least three subcutaneous injections of the undiluted toxin in graduated doses, and, second, that this immunity can be produced against the toxin of one type by injections of a mixture of toxins of all types.

While the results of these tests indicate certain facts in regard to the stimulation of active immunity in man against meningococcus toxin, they do not necessarily signify that an immunity against the organism can be produced at the same time, although such a condition is true of some soluble toxins and it is not unreasonable to expect the same of this toxin. This method of immunization, however, does suggest a possible means of active protection against the disease itself and is worthy of consideration and further study, especially since it was shown in a previous paper in this series that active immunity against infection with the virulent meningococcus can be stimulated in laboratory animals following prophylactic injections of this toxin. The answer to this question, while of great importance, must of necessity be deferred until such a time as more conclusive clinical data are available.

4. Ferry, N. S.: Meningococcus Antitoxin: II. Therapeutic Tests on Monkeys, J. Immunol. **23**: 325 (Oct.) 1932.

5. This work was carried out at the Wayne County Training School, through the courtesy of Dr. Robert H. Haskell, superintendent.

VERRUGA PERUANA (CARRION'S DISEASE)

BASED ON PERSONAL EXPERIENCE IN PERU

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My principal object in a recent visit to Peru was to obtain first hand information of the cutaneous lesions of the disease known in that country as verruga peruana. To understand fully its eruptive phase it is necessary to give a general description of this fascinating and unique disease.

Before the causative organism was successfully cultivated, there was some doubt about the relationship of what was called Oroya fever and the cutaneous eruption known as verruga. As it has now been proved beyond any possibility of doubt that these two supposedly different disorders are in reality the same disease, it is perhaps best to characterize the entire process as Carrion's disease, in honor of the young student who lost his life after a voluntary inoculation.

HISTORY OF THE DISEASE

Carrion's disease probably existed in remote times and is generally thought to have been known to the Spanish conquerors of Peru. According to Maldonado,[1] however, the condition described by the conquerors as berruga was in reality not verruga but yaws, and its first authentic mention should date from 1630.

Fig 1 (case 1).—Profuse miliary eruption of three months' duration, preceded by fever and joint pains, in a man, aged 21. Lesions show a slight tendency to coalesce. Many are covered with blood crusts. The lesions are mostly yellowish red, some being bright red.

Previous to 1870 little was known of the disease. At that time the transandean railway to the town of Oroya was begun and this was followed by a disastrous epidemic. It has been estimated that there were at least 7,000 deaths among those engaged in this railroad construction, most of the laborers being Chileans. The term Oroya fever by which the disease was known is not appropriate, as it has never been seen in Oroya.

Opinions differed regarding this terrifying disease. Some thought it an entirely new disease, others a modified form of malaria or other disorder. Some concluded that Oroya fever was a severe form of verruga.

The view that Oroya fever and verruga were the same disease gained ground until 1885, when the question was apparently settled in its favor by the experiment of Daniel A. Carrion. In his desire to study the symptoms and sequelae of the disease, Carrion insisted on being inoculated from a case of verruga. Unfortunately he contracted the serious type (Oroya fever) and died thirty-nine days after inoculation. Carrion is rightly regarded by his fellow countrymen not only as a most courageous man but also as one of considerable scientific attainments. He proved that verruga was inoculable in human beings and that in all probability verruga and Oroya fever were different phases of the same disease. As Odriozola [2] says, the case was similar to "variolac sine variolis" or "rubeolae sine rubeolis."

Fig. 2 (case 1).—Variation in size of lesions and tendency for older ones to be pedunculated.

In arriving at the important conclusion that Oroya fever and verruga were independent conditions, Strong and his co-workers [3] of the Harvard expedition to South America were doubtless influenced by their failure to find the record of Carrion's experiment. The detailed account of Carrion's illness and autopsy were, however, published by Alcedan [4] in 1903. The opinions of the members of the Harvard expedition, consisting of four Americans and one Peruvian, all of the highest reputation, carried great weight, though their main conclusion was later proved to be erroneous.

GEOGRAPHIC DISTRIBUTION

Carrion's disease is unique in its geographic distribution, being in all probability confined not only to Peru but to certain restricted areas in that country. It occurs between 8 and 13 degrees south latitude and at an altitude varying from 2,800 to 9,000 feet. The coastal and high mountainous regions are free. The disease appears only on the western slope of the Andes, in certain narrow ravines or canyons with luxuriant vegetation and considerable heat during the day. The small towns and villages where the disease is prevalent are sheltered from strong winds (which would affect insect life), as the ravines are at right angles to the prevailing winds.

SYMPTOMS OF MALIGNANT TYPE (OROYA FEVER)

It is convenient to describe separately the symptomatology of the malignant type (formerly known as

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1. Maldonado, A.: La berruga de los conquistadores del Peru Cronica med. (Lima) **48**: 313 (Oct.) 1931.

2. Odriozola, E.: La maladie de Carrion. Paris, Carré et Naud, 1898.

3. Strong, R. P.; Tyzzer, E. E.; Sellards, A. W.; Brues, C. T., and Gastiabaru, J. C.: Harvard School of Tropical Medicine, Report of First Expedition to South America, Cambridge, Mass., Harvard University Press, 1915.

4. Alcedan, M.: Enfermedad de Carrion, Crón. méd., Lima **3**: 381 (Oct. 31) 1886.

Oroya fever) and the benign eruptive type (verruga), although there are innumerable gradations between them.

The incubation period is not definitely known, Odriozola estimating it to vary between fifteen and forty days. In the experimental infection of Carrion it was twenty-one days. After a prodromal period of malaise, headache and muscle pains there is a sharp rise of temperature accompanied by chills. Fever is most often of the remittent type. It may disappear for several days and be followed by subnormal temperature, profound weakness and death. When it lessens proportionately with amelioration of all symptoms, the outlook for recovery is almost certain.

Fig. 4 (case 2).—Miliary eruption with scaling and a few blood crusts.

A striking feature is the rapidity with which profound anemia appears. There is probably no condition except hemorrhage that can cause severe anemia so quickly. The red cells may decrease to one million per cubic millimeter within three or four days, though this usually takes place in from one to two weeks.

The blood change is a combination of pernicious anemia and leukemia. The anemia is due, as Monge [5] states, to a disturbance in the regenerative capacity of the blood rather than to its destruction, as there is neither hemorrhage nor any sign of hemolysis in proportion to the diminution of the red cells. Both normoblasts and megaloblasts are numerous in the peripheral blood and have a prognostic as well as a diagnostic importance, the prognosis being better with a decrease of the megaloblasts compared with the normoblasts. The blood also shows in severe cases all the bizarre forms of pernicious anemia. The leukocytes are increased at first and may reach 20,000 per cubic millimeter. The eosinophils disappear and there may be myelocytes and myeloblasts in the peripheral blood. The red cells in addition show large numbers of Bartonella bacilliformis, the causative organism.

Fever and anemia are accompanied by severe anorexia, unquenchable thirst, muscle and joint pains, vomiting, hiccups, attacks of syncope and delirium. Epistaxis and petechiae are common, the latter being the earliest stage of verruga papules. Estimates of mortality vary from 30 to 98 per cent.

SYMPTOMS OF BENIGN TYPE (VERRUGA)

The symptoms of benign (eruptive) type also vary greatly. In infants and young children they are mild or often trifling, as I had occasion to observe on my trips to the Rimac valley.[6]

The period of incubation is not known precisely. According to Arce it is usually between twelve and forty days. In experimental inoculations in animals it varies from eight to sixty days. Two periods of evolution of the disease are described: (1) invasion (preeruptive) and (2) eruptive.

The period of invasion begins with malaise, gastrointestinal disturbances and fever, with more or less intense pain in the muscles and joints, especially of the extremities. Fever, according to Odriozola, is always present and is usually of intermittent or tertian type, stopping a few days before the cutaneous outbreak. Pain and edema are in direct proportion to the severity of the eruption. The blood shows simple anemia and may contain the causative organism in considerable numbers. The average duration of this period is stated by Odriozola to be from three to four months.

Before discussing the eruption of verruga it should be said that the Spanish word verruga is the equivalent of the Latin word verruca, meaning wart. Verruga is an unsatisfactory term, as the lesions seldom have any clinical and never any histologic resemblance to ordinary warts. The word verruga, in common use by the public, corresponds, I should say, to the English word pimple.

The cutaneous lesions are of two main types: (1) miliary, which are situated in the cutis, and (2) nodular, which arise in the subcutaneous tissue. A subvariety of the nodular type is spoken of as "mula" or mular, to anglicize the word, derived from the fact that mules suffer from the same disease.

Miliary Type of Eruption.—The term miliary is not very suitable, as the lesions vary in size from a small pinhead to a good sized split pea. The eruption, for instance, hasn't the remotest resemblance to the miliary papular syphilid. In general it is symmetrical, particularly when it is profuse.

The favorite sites are the extensor surfaces of the extremities and next in frequency the face and neck. The trunk is usually spared unless the eruption is very profuse. The palms and soles are usually free, and the genitalia are infrequently attacked, though I photographed one patient with numerous papules on the penis and scrotum. There is a great variation in the number of lesions. Some infants and young children whom I saw in the Rimac valley had only a half dozen papules, while two cases studied in the Dos de Mayo Hospital in Lima (through the courtesy of Drs. Gonzales Oleachea and Voto Bernales) presented profuse eruptions (figs. 1 to 5).

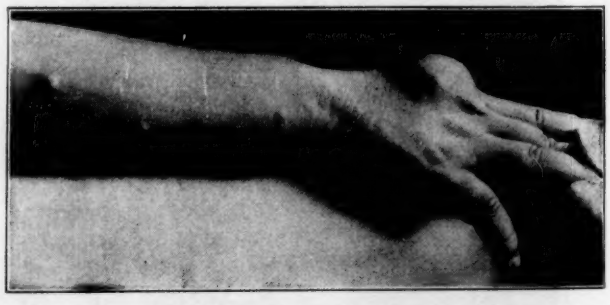

Fig. 6 (case 3).—A large nodule appeared over the first metacarpal bone of three months' duration, not preceded by any constitutional symptoms, in a girl, aged 10 months. The nodule was hemispherical, hard and painless and covered by normal skin, freely movable over it. There were also a few miliary lesions on the face and two on the forearm, as shown in the illustration.

As a rule, the lesions are discrete and often closely aggregated, but at times they show a slight tendency to coalesce. They are said to arise on tiny petechial spots and to increase gradually in size. It is also stated

5. Monge, C. M.: Verruga peruana o enfermedad de Carrion, Beihefte z. Arch. f. Schiffs- u. Tropen-Hyg. **29**: 244, 1925.

6. Through the kindness of Dr. E. A. MacCornack, who aided me in every possible manner, I was able to motor up the Rimac valley and visit the towns of Matucana, Surco and St. Bartolomé.

that they occasionally begin as minute vesicles or even pustules. Some of them do not attain full pea sized development, and in all cases a striking feature is the difference in the size of the lesions. This is due to their appearing in crops at varying intervals. At the outset they are all sessile, hemispherical or rounded elevations, some of them eventually becoming more or less pedunculated.

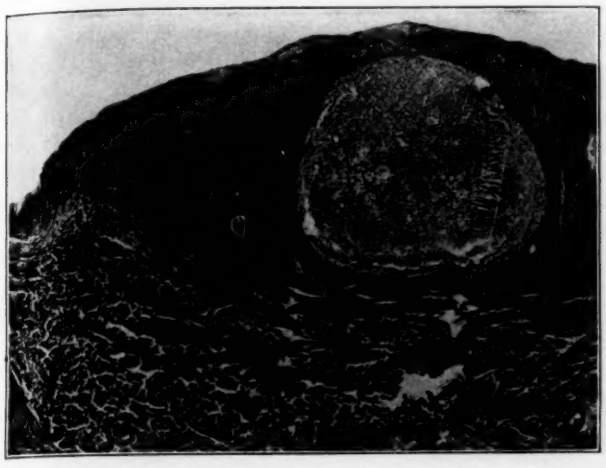

Fig. 7 (case 2).—Section of early miliary lesion in upper corium almost entirely encircled by acanthotic rete, under low power. Shows proliferation of capillaries, many of which are dilated.

The color is also extremely variable, many of the lesions having a faint pinkish hue while others stand out in bold relief from the pronounced reddish color of varying shade. Some are bright red like little senile angiomas. Their vascularity is evident from the number of blood crusts that are noted, bleeding readily taking place from slight trauma or scratching. From some descriptions and a colored illustration in Odriozola's monograph one would get the impression that all the lesions were bright red. This was certainly not so in my limited experience. The skin between the individual lesions is normal in appearance.

The consistency of the miliary verrugas is hard at the outset and in many small lesions could, I think, be properly described as shotty. As the lesions increase in size and age they become distinctly softer. The overlying skin is smooth and tense in the small lesions, but later in the stage of retrogression it may appear wrinkled or covered with blackish blood crusts.

Subjective symptoms are not a feature of the disease. At the outset a pricking sensation may accompany the appearance of petechiae and in the stage of retrogression an annoying amount of itching may be present.

The duration of the eruption is variable. Odriozola estimates it to be from four to six months on the average, though he states that he has seen a case in which the eruption lasted more than two years. The lesions eventually disappear with or without desquamation and leave no scarring or pigmentation.

Nodular Type of the Eruption.—The nodular type is less frequent and the lesions are much less profuse than those of the miliary type. They originate in the subcutaneous tissue as little hard rounded bodies, which at first cause no elevation of the skin. They can be palpated before they are visible. It is said that they are somewhat tender, though this was not apparent in cases that I observed. The lesions may disappear without enlarging or may increase in size and cause a varying degree of elevation covered by skin that is normal or somewhat reddish. The favorite sites are the extensor surfaces of the extremities. An example of a well developed large nodule is shown in figure 6.

The so-called mula lesion is merely a large nodule that has broken through the overlying skin and in which secondary infection often takes place. Such lesions are either sessile or pedunculated, are firm and elastic, bleed easily and vary in size from a small nut to a small apple. They occur especially on the knees, though also on other regions including the face, and may be accompanied by severe hemorrhage, which endangers the patient's life. These lesions are uncommon and I had no opportunity to see them.

In addition to the skin, the mucous membranes of the conjunctiva, nose, mouth, pharynx and gastrointestinal tract may be the sites of verruga nodules.

The prognosis of the eruptive type of Carrion's disease is nearly always favorable, especially when a generalized eruption appears rapidly and disappears slowly, accompanied by an improvement in the general condition.

Differential Diagnosis of Cutaneous Lesions.—The diagnosis is usually easy when one has seen a number of undoubted cases. The eruption as a whole is unique and unlike any disorder of the skin with which I am familiar. Some individual lesions look precisely like granuloma pyogenicum, but I think the eruption as a whole is rather suggestive of multiple sarcomatosis,

Fig. 8 (case 2).—Appearance under high power, showing increase in number of capillaries of small caliber, marked proliferation of cells of the reticulo-endothelial system, and hemorrhage (erythrocytes in the lumens and dispersed among the cells of the infiltration).

especially in the earlier stages before any of the papules have become pedunculated. Jadassohn saw a Swiss guide in Bern who had contracted the disease while climbing in the Andes and stated that the eruption suggested multiple angioma, hemorrhagic sarcoma or telangiectatic (pyogenic) granuloma. Needless to say,

mistakes in diagnosis are made by the public in the verrugous districts and even by physicians. A patient whom I saw at Surco stated that he was suffering from verruga. If I had seen this man in the United States I would have considered his eruption to be a typical molluscum contagiosum. I still feel doubtful about this case.

EPIDEMIOLOGY

Carrion's disease occurs in both sexes, in all races and at all ages. It may appear in the new-born, when it is usually of severe type. Odriozola quotes a single case of apparent intra-uterine infection. The disease is, however, not hereditary in the strict sense of the word. It is inoculable but not contagious.

In the verrugous zones, practically all natives are infected in infancy or early childhood and are thereafter immune. Gomez,[7] from an extensive epidemiologic study, concludes that in the first years of life (up to ten or more years) the disease is almost always of the benign type, tending to acquire extreme severity in adolescence and adult life. In the Rimac valley, I saw five infants from 8 to 9 months of age, all of whom presented sparse but typical eruptions and appeared in perfect health. In no case was there a history of any but the mildest constitutional disturbance before the appearance of the eruption. A day or two of malaise or fever had been noted by some of the mothers. Most of the well marked cases of the disease are seen in strangers who visit the verrugous regions and remain there during the night. While one attack confers lasting immunity, there are occasional recurrences. Odriozola refers to cases in which this took place three and five years respectively after infection. In a personal communication, Dr. Edmundo Escomel states that he has recently seen a mular type of lesion on the great toe of an individual who had been infected with verruga eighteen years previously. The verrugous nature of the lesion was proved histologically. While the disease may be acquired at any time of year, the majority of infections occur between the months of December and March.

BACTERIOLOGY

Alberto Barton[8] in 1909 expressed the view that bacillus-like bodies which he had previously described in the erythrocytes of cases of the malignant type of Carrion's disease were the probable cause of the disease. These bodies were later named Bartonella bacilliformis by Strong and his co-workers, and they have been definitely proved to be the causative organisms. They are thought to be bacteria by Noguchi[9] and by Aldana.[10]

The organisms are best seen in smears stained by the Giemsa method and appear as rounded or rod shaped bodies, the rodlike forms measuring from 1 to 2 microns in length and from 0.2 to 0.5 micron in width. They appear singly, in pairs and in end to end chains and frequently assume a V or Y form. The round bodies measure from 0.3 to 1 micron in diameter and occur isolated or in groups. A red cell may contain one or many organisms.

According to Aldana, Bartonella bacilliformis is not an endoglobular parasite, as has formerly been considered. In his opinion it is merely adherent to the red cell, its situation on the cell being accidental and due to breaking up of endothelial cells of the blood capillaries. Bartonella, he says, does not destroy the red cell, nor does it require these cells for its multiplication.

Bartonella bacilliformis is seen not only in the peripheral blood but in most of the tissues and organs of the body. It has doubtless been observed in the cutaneous lesions, a fact of great importance as another proof that so-called Oroya fever and verruga are the same disease. At least it can be said that bodies indistinguishable from Bartonella have been found in the verruga lesions. These were first described in 1913 by Mayer, da Rocha Lima and Werner[11] as inclusion bodies closely resembling parasites of the chlamydozoa group. Their presence was later confirmed by Mackehenie and Battistini,[12] and in experimentally produced lesions by Mackehenie and Weiss[13] and by Marques da Cunha and Muniz.[14]

Cultures.—In his most recent and excellent article on Carrion's disease, da Rocha Lima[15] states that Bartonella bacilliformis was first cultivated by Noguchi and Battistini in 1926. This is not entirely correct, as the records show that Battistini[16] reported successful cultures in 1925. It is also stated that Hercelles cultivated the organism in the same year.

Bartonella bacilliformis is a gram-negative, obligate aerobe, which is usually nonmotile. It grows in solid or liquid mediums containing whole blood, plasma or serum (Aldana) and only below 37 C. The organism may be isolated by blood cultures from patients in both anemic and eruptive stages and even at times after the disappearance of the eruption.

HUMAN INOCULATIONS

Mention has already been made of the experiment practiced on himself by the young student Carrion. The inoculation was made under protest by his friends, who realized his danger. Thinking that this memorable experiment settled the question of unity of the two types of the disease and realizing the danger of human inoculations, Peruvian physicians have refrained from carrying out further experiments on man.

Strong and his co-workers inoculated a volunteer Chilean with material taken from two cases of verruga. On the sixteenth day cherry red papules appeared at the site of the inoculation and were histologically "similar to other early human lesions of the disease." There was no appreciable anemia and the blood showed no Bartonella. From this experiment they concluded that "direct inoculation of the verruga virus from man to man does not produce Oroya fever." As a matter of fact, it merely showed that inoculation of verruga material could produce verruga.

An accidental inoculation of a Peruvian physician furnished another proof of the identity of so-called Oroya fever and verruga peruana. The procedure in this case was the reverse of Carrion's experiment. This physician (O. G. R.) gave me the following description

7. Gomez, M. E.: Epidemiologie del enfermedad de Carrion en las Provincias de Yauyos Canete, Crón. méd., Lima **31**: 53 (Feb.) 1914.
8. Barton, Alberto: Crón. méd., Lima **26**: 7, 1909.
9. Noguchi, Hideyo: The Etiology of Verruga Peruana, J. Exper. Med. **45**: 175 (Jan.) 1927.
10. Aldana, G. L.: Bacteriologia de la enfermedad de Carrion, Crón. méd., Lima **46**: 235 (Aug.) 1929.
11. Mayer, Martin; da Rocha Lima, H., and Werner, H.: Untersuchungen über Verruga peruviana, München. med. Wchnschr. **60**: 739 (April) 1913.
12. Mackehenie, D., and Battistini, T. S.: Contribucion al estudio de la Verruga Peruana, Bol. Soc. Peruana Para el Progreso de la Ciencia, August 1912.
13. Mackehenie, D., and Weiss, P.: Contribucion al estudio de la Verruga Peruana, Beihefte z. Arch. f. Schiffs- u. Tropen-Hyg. **29**: 211, 1925.
14. Marques da Cunha, A., and Muniz, J.: Untersuchungen über die Verruga Peruviana, Mem. do Inst. Oswaldo Cruz. **21**: 167, 1928.
15. da Rocha Lima, H.: Verruga Peruviana oder Carrionsche Krankheit (Oroya Fieber), Handb. d. Haut- u. Geschlechtskr. **22**: 215, 1932.
16. Battistini, T. S.: Contribucion al estudio de la Verruga Peruana: Nota Preliminar, An. Fac. de med., Numero Extraordinario, Oct. 1, 1925, p. 27.

of his infection. He was accidentally inoculated in February 1931 by a needle prick while giving a blood transfusion to a patient with the malignant type of Carrion's disease. Fever appeared eight days later without premonitory symptoms and rose to 40.4 C. (105 F.). During the following three weeks it continued with slight remissions between 38 and 39 C. (100.4 and 102.2 F.). The blood showed four million red cells and 4,800 leukocytes. Ten days after the disappearance of the fever he suffered from intense pains in the extremities. Several days later there was an eruption both of miliary and of nodular type, which disappeared at the end of ten months and did not recur.

ANIMAL INOCULATIONS

It is the consensus in Peru that many animals suffer spontaneously from the eruptive type of verruga, though little study of this question has been made. The fact that various animals can be artificially infected is, as has been said, no proof that they acquire the disease naturally.

The first undoubted transference of the disease to animals was made by Jadassohn and Seiffert,[17] who in 1910 inoculated monkeys and carried the infection through three generations. Subsequent successful inoculations in monkeys were made by Mayer, by da Rocha Lima and Werner, by Arce, Mackehenie and Ribeyro,[18] by Strong and his co-workers, by Noguchi, and by others. Other animals that have been successfully inoculated include the dog, sheep, goat, ass and rabbit (intratesticularly).

Further proof that Oroya fever and verruga are the same disease is shown by the following animal experiments: In two monkeys inoculated locally from verrugous lesions by Mayer and Kikuth [19] there were severe fever and anemia with changes precisely like those in man, with swarms of Bartonella in the blood and a fatal termination. Noguchi [20] also showed that Rhesus monkeys that have recovered from infection with the Oroya strain of Bartonella are completely immune to the verruga strain.

Experimental animal infections have usually been obtained by direct inoculation of verrugous material in the skin, less often by cultures and almost never with blood, even when it swarms with Bartonella. Mayer and Kikuth observe in this regard that "further cultural experiments and inoculations should show whether all the developmental stages of the virus are communicable and whether various diseases or conditions are necessary (condition of the reticulo-endothelial system and injury from other infections)."

TRANSMISSION BY PHLEBOTOMUS

The first suggestion that Carrion's disease might be transmitted by some blood sucking insect was made by Arce in 1889. The first extensive investigations were made by Townsend,[21] who worked for two years (1912-1914) in the Rimac valley. He demonstrated conclusively that the disease is transmitted by a species of phlebotomus, which he named P. verrucarum. He was able to exclude mosquitoes, flies, fleas, lice, bedbugs, ticks and mites as possible vectors.

Shannon [22] later corroborated Townsend's views regarding transmission and added another new species of phlebotomus as a vector, which he named P. Noguchii.

The following ecologic evidence that phlebotomus is the vector of verruga was stated by Shannon: As the disease is contracted only in certain zones, during the night (with possible exceptions) both indoors and far from habitation, at any time of the year, he concluded that the vectors must be common blood suckers of man, restricted to verruga zones, nocturnal in habits and able to breed in unrestricted situations. In order that the adults (which have a very restricted flight) may be practically omnipresent, they must continue active throughout the year.

According to Shannon, P. verrucarum and P. Noguchii conformed to all these requirements, while all other blood sucking arthropods could be excluded. P. verrucarum, he stated, appeared to be predominantly a domestic species, while P. Noguchii occurred consistently outdoors. This probably explains, Shannon stated, why the disease may be contracted indoors and outdoors, at times miles from any habitation.

POSSIBLE RESERVOIR OF VIRUS

As certain native and domestic animals in the infected zones are susceptible to the disease, Townsend thought there was apparently no need of a natural reservoir and possibly, he said, none exists. He then made the following significant statement: "It seems curious that man becomes so quickly infected when there is such a comparatively sparse animal and human population existing in most parts of the region." He added "Possibly there are other sources from which they obtain the infectious material." The possible sources may be certain lactescent plants, as indicated in the following paragraphs.

After a careful study of the plant life in certain verruga canyons, Maldonado [23] in 1930 found that certain plants were characteristic of these zones and that they did not exist in nonverrugous areas. This suggested that they might play some causative rôle, first as a reservoir of the virus and secondly as food for the insect vector. The plants in question were the lactescent ones commonly known as huanarpo macho (Euphorbiaceae family) and the huancoy (Julianaceae family). He subsequently [24] (1932) affirmed that the conditions necessary for the lactescent vegetation and the phlebotomus are the same in whatever part of Peru they may be studied.

Mackehenie and Coronado [25] in January 1933 found in the juice of specimens of huanarpo macho bodies very similar to Bartonella, when using appropriate stains. Under aseptic precautions, cultures were obtained from the latex of the plant showing the characteristics of Bartonella. Cultures from another species of euphorbia, when injected into the anterior chamber of a white rabbit, caused an iridocyclitis, from which the organisms were cultivated and found pathogenic

17. Jadassohn, J., and Seiffert, G.: Ein Fall von Verruga Peruviana: Gelungene Ubertragung auf Affen. Ztschr. f. Hyg.- u. Infektionskr. **66**: 247 (July) 1910.

18. Arce, J. N.; Mackehenie, D., and Ribeyro, R. E.: Estudio Experimental de la Enfermedad de Carrion, Crón. med., Lima **30**: 394 (Oct.) 1913.

19. Mayer, Martin, and Kikuth, Walter: Zur Aetiologie und Einheit der Verruga Peruviana und des Oroyo Fiebers, Arbeiten über Tropenkrankheiten u. deren Grenzgebiete, Hamburg, 1927, p. 319.

20. Noguchi, Hideyo: Experiments on Cross Immunity Between Oroya Fever and Verruga Peruana, J. Exper. Med. **45**: 781 (May) 1927.

21. Townsend, C. H. T.: Two Years Investigation in Peru of Verruga and Its Insect Transmission, Am. J. Trop. Dis. **3**: 16 (July) 1915.

22. Shannon, R. C.: Entomological Investigations in Connection with Carrion's Disease, Am. J. Hyg. **10**: 79 (July) 1929.

23. Maldonado, A.: Probable rol de algunas plantes lactescentes, caracteristicas de las Quebradas Verrucogenas y utogenas, Crón. méd., Lima **47**: 381 (Dec.) 1930.

24. Maldonado, A.: Nuevo Criterio para explicar la distribucion geografica de la enfermedad de Carrion, Crón. méd., Lima **50**: 41 (Feb.) 1933.

25. Mackehenie, D., and Coronado, D.: Plantas reservorios de Virus: Contribucior. al conocimiento de la fitopatogenesis Peruana, Rev. méd. peruana **5**: 803 (May) 1933.

for guinea-pigs. The authors also observed small insects on the trunks of these plants belonging possibly to the family of psocidae. Organisms found in the digestive tract of these insects were easily cultivated and were virulent to a guinea-pig that suffered from nervous symptoms, including paralysis. Agglutination was obtained by the plant virus and that from the insects in contact with serum from a convalescent verruga patient in two cases at a dilution of 1 to 1,600. The authors concluded that the organisms obtained from the latex of the plants and from the insects could be placed in the genus Bartonella, based on their morphology and experimental reactions. Monkeys were unfortunately not available at the time for experimentation.

PATHOLOGY

According to Hercelles,[26] hemorrhage and thrombosis are the principal changes that are constantly present in the malignant type. Most of the tissues and organs may be affected. Bartonella has been cultivated from many of them, notably the kidneys, lymphatic glands, spleen and bone medulla.

Weiss [27] speaks of the two types of the disease as hematic and histioid. The former is characterized by the presence of Bartonella in the circulating blood. In the histioid type the organisms limit their activity to the reticulo-endothelial system and cause degenerative-exudative reactions. He considers the formation of verrugous (eruptive) lesions to be an allergic reaction to the virus. It is interesting to note that in the histioid stage Weiss was able to show verrugous changes in the skin microscopically before they were macroscopically visible.

Histopathology of Verruga Lesions.—Opinions about the histologic structure of verruga lesions have varied, some of the earlier investigators considering them to be a fibrosarcoma or suggestive of either sarcoma or angioma. Hercelles [28] thought that they were of vascular origin, due to periarteritic proliferation. Escomel [29] considered the process to be inflammatory rather than neoplastic and thought what he termed "verruga cells" to be the characteristic element and that they arose from connective tissue cells.

Cole [30] thought that the lesions were granulomas with special histologic changes, characterized by dilatation of lymph vessels and choking of their lumens with mononuclear and polymorphonuclear leukocytes. There was also perivascular infiltration of plasma cells, fibroblasts, mononuclear and relatively few polymorphonuclear leukocytes and the formation and dilatation of many blood capillaries with marked edema and extravasation of red cells in the tissue.

Strong and his co-workers summarize the changes as follows: "The verruga nodule constitutes a special form of granuloma characterized in the early stages by the formation of new blood vessels in edematous connective tissue and by marked proliferation of the angioblastic cells forming masses or islands of closely placed cells, by the invasion of the connective tissue by lymphocytes, plasma cells and leukocytes and as the lesion progresses by the formation of fibroblasts and the deposit of collagen fibrils." They stated that the verruga tissues may have at times a sarcomatous, at times a myxomatous or at times an angiomatous (cavernous) appearance.

Rocha Lima, who has written extensively on this subject, summarizes the histogenesis of the verruga lesion in saying that the "basic process in the formation of verruga tumors is a growth of vascular elements."

HISTOLOGIC EXAMINATIONS

Three biopsies were obtained from two patients, the histologic examinations being made by Dr. T. J. Riordan.[30a]

TREATMENT

Treatment is purely symptomatic, no specific drug or vaccine having been found to be of real value, though Arce [31] (quoted by Noguchi) recommended small doses of arsphenamine. Blood transfusions have proved to be very disappointing and in the opinion of some Peruvian physicians are contraindicated. Blood from a nonimmune donor, according to Weiss, acts like a culture medium for the organisms. It would be interesting, he says, to try the effect of blood from an individual in the histioid (eruptive) stage.

Prophylaxis is all important and consists chiefly in remaining away from verruga zones from sundown to sunrise. According to Townsend, no one has ever been known to acquire the disease unless he has spent one or more nights in infected districts.

SUMMARY

The diseases formerly known as Oroya fever and verruga peruana have been definitely proved to be phases of a single process, conveniently called Carrion's disease. They are restricted to certain parts of Peru and present several unique features. The malignant type (Oroya fever) shows a profound anemia occurring more rapidly than in any condition except hemorrhage, and the eruptive stage (benign type) differs from all known skin diseases. The causative organism (Bartonella bacilliformis, Strong) has been demonstrated morphologically and by culture in the circulating blood, inner organs and eruptive (verrugous) lesions. Infection with one type is followed by immunity to the other, both in human and in experimental animal infections. Human and animal inoculations of one type may produce the other type of the disease. The insect vector (certain species of phlebotomus) has been discovered and possibly the existence of a plant reservoir. There is no specific treatment.

In addition to help from physicians mentioned in the text, I received advice and assistance from Drs. Monge, Barton, Escomel, Hercelles, Mackehenie and Weiss.

140 East Fifty-Fourth Street.

ABSTRACT OF DISCUSSION

DR. HAROLD N. COLE, Cleveland: There will probably not be many cases of verruca peruviana encountered in the United States, but once in a while one of them wanders into Panama or somewhere in the Southern states. There is no question about the condition being a very characteristic granuloma in its clinical and also its histologic appearance. One who has studied a case will never forget the formation of new vessels, the hemorrhage into the tissues, the eosinophilia fibroblast and plasma cell infiltrations in the local tissues. I think it is well that Dr. Fox has brought out the change in conception since

26. Hercelles, O.: Enfermedad de Carrion, Crón. méd., Lima **31:** 67 (March) 1914.
27. Weiss, P.: Contribucion al estudio de la verruga peruana o enfermedad de Carrion, Rev. méd. latino-am. **18:** 1121 (July) 1933.
28. Hercelles, O.: La anatomia patologica de la verruga, Quinto Congreso Med. Latin Amer. Lima, Peru, Vol. **2.** Nov. 9, 1913.
29. Escomel, Edmundo: Anatomie pathologique du verrucome de Carrion, Ann. de dermat. et syph. **3:** 961 (Nov.) 1902.
30. Cole, H. N.: Verruga Peruana: Its Comparative Histological Study in Man and the Ape, J. Cutan. Dis. **31:** 384 (June) 1913.

30a. The report of these examinations will appear in the author's reprints.
31. Arce, J.: Ann. Fac. de med., Lima, No. 4, 24-52, 1918.

the report of the Harvard commission. After the Harvard commission came back, Dr. Strong kindly sent me a copy of its monograph, and apparently it had drawn some wrong conclusions and felt that the diseases were separate, while it seems that they actually are the same condition. I was interested in Dr. Fox's remarks in regard to the mild type of the disease in little children. I was wondering whether possibly these children, owing to the influence of the mother's blood, because all the inhabitants in that neighborhood have had the disease, might show a certain resistance to the disease and therefore contract it simply in a mild form. It is a most interesting problem for the immunologist, and I predict that one of these times another commission is going to be sent down there and it will work out some method of taking care of the population and ridding it entirely of this disease.

DR. HOWARD FOX, New York: In the time at my disposal I could only touch on the more important points. The eruption of verruga peruana is unlike anything I have ever seen. Some of the lesions look like angioma and some like granuloma pyogenicum, but taken as a whole it suggests a generalized sarcomatosis in many ways. Dr. Cole's question as to why children have such a mild attack is one that I cannot answer. I had previously asked the same question of some Peruvian physicians, who could give no answer to it.

EPIDEMIOLOGIC FACTORS IN MEASLES PROPHYLAXIS

SAMUEL KARELITZ, M.D.
AND
BELA SCHICK, M.D.
NEW YORK

In using immune adult blood serum in the prophylaxis of measles, we observed that the interpretation of our results depended largely on whether certain epidemiologic factors were taken into account. Under relatively constant conditions the results obtained in institutional exposures seemed good; the percentage of complete protections was high, whereas under similar conditions, with the exception that the children were exposed to their sick siblings at home after prophylactic treatment, the percentage of protections was very much smaller. We have therefore divided 263 cases treated with immune adult serum according to the circumstances of their exposure to measles in an attempt to answer the following questions:

1. How do the results obtained with serum injected prophylactically into children exposed to measles in institutions compare with those obtained under similar conditions in private homes; that is, in children exposed to their sick siblings and treated at home?

2. Can this difference be obviated or reduced by increasing the size of the dose or the potency of the serum?

3. Are the results in all homes the same, or do they vary with the hygiene?

INJECTION OF SERUM IN HOSPITAL AND IN HOME

The cases treated with the serum obtained from five blood donors are charted (chart 1) according to whether they were exposed to measles while in institutions or to sick siblings at home. It is evident that, with the same dosage of serum injected in children of comparable ages and exposed to measles for similar periods, the percentage of presumably protected cases was greater in hospitals than in homes. This was true for each of the five donors. Compositely of 134 cases there were 87 per cent protections in hospitals against 29 per cent in homes, the modifications were 13 per cent in hospitals and 22 per cent in homes, and the failures were 0 per cent in hospitals and 49 per cent in homes (chart 2, columns 1 and 2).

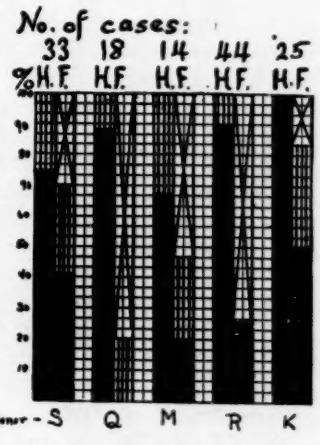

Chart 1.—Results of use of serum of individual donors in homes as compared to hospitals; conditions otherwise similar. In these charts the solid black column indicates protected cases; vertical lines indicate modified cases, and the crossed column indicates unprotected cases; *H*, hospital cases, and *F*, familial or home cases.

A few specific experiences may serve well in illustrating the point just made. In an outbreak of measles among the 3 year old children at the S. V. Hospital, eighteen children were each injected with 6 cc. of serum obtained from donors Q and R. All remained free of measles. In one control case the disease developed. At the B. J. Hospital ten out of twelve children, each injected with 6 cc. of K serum, remained well; in one child typical measles developed and in one the modified type of the disease. Although the results seem excellent and although in previous outbreaks of measles at the B. J. Hospital there were usually 100 per cent cross infections, comparison of these results with those obtained with the same serum injected in patients exposed at home (chart 2, columns 1 and 2) shows a striking difference, the percentage of protections being very much less in the latter group.

We may infer corroboration of our results from the report of Park and Freeman,[1] which reveals that of 652 patients exposed from one to six days in institutions and injected (chart 2) with 6 cc. of convalescent serum, 91 per cent were protected, 7 per cent of the cases were modified and only 2 per cent were unaided, whereas of 226 patients treated at home under otherwise similar conditions, only 52 per cent were protected, but 42 per cent of the cases were modified. The data of Levinson and his co-workers[2] for convalescent serum used in homes are very similar to those of Park and Freeman.

TABLE 1.—*Results of Use of Serum of Individual Donors in Homes as Compared to Hospitals: Conditions Otherwise Similar*

Donor	Protected		Modified		Failed	
	Hospital	Home	Hospital	Home	Hospital	Home
Sacks	12	7	4	5	0	5
Quinn	7	0	1	2	0	8
Messer	2	2	1	3	0	6
Robinson	26	4	3	0	0	11
Karelitz	13	6	0	4	0	2
Total	60	19	9	14	0	32
	87%	29%	13%	22%	0%	49%

This work was aided by a grant from the Emilie Fries Fund.
From the Department of Pediatrics of the Mount Sinai Hospital.

1. Park, W. H., and Freeman, R. G., Jr.: Prophylactic Use of Measles Convalescent Serum, J. A. M. A. **87**: 556 (Aug. 21) 1926.
2. Levinson, S. O.; McDougall, C., and Thalling, W.: The Use of Convalescent Serum for the Prevention and Attenuation of Measles, Illinois M. J. **63**: 258 (March) 1933.

SIZE OF DOSE OR POTENCY OF SERUM

It seemed reasonable to expect that by increasing the dosage of the serum employed an amount would be reached at which practically no difference would be observed in the percentage of protected cases in hospitals and in homes. Chart 2, columns 2, 3 and 4, demonstrates that this prediction was warranted. The first two columns indicate that in 134 cases, quite similar to the group referred to in chart 1, the results were very much alike; 83 per cent of the cases treated with 6 cc. of serum in hospitals were completely protected and 17 per cent were modified. In homes with similar dosage the completely protected were 29 per cent, the modified 22 per cent and the failures 49 per cent of the cases. When the dosage of serum was increased to 8 cc. (column 3) and was tested only in homes, there was a rise of protected cases from 29 per cent to 46 per cent and in modified cases from 22 per cent to 43 per cent. The failures dropped from 49

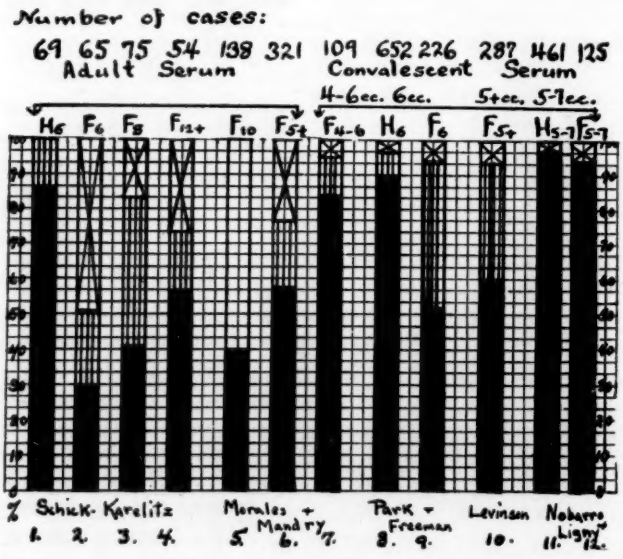
Number of cases:
69 65 75 54 138 321 109 652 226 287 461 125
Adult Serum
Convalescent Serum
4-6cc. 6cc. 5+cc. 5-7cc.
H6 F6 F8 F12+ F10 F5+ F4-6 H6 F6 F5+ H5-7 F5-7
%
Schick-Karelitz
Morales + Mandry
Park + Freeman
Levinson
Nabarro Signy
1. 2. 3. 4. 5. 6. 7. 8. 9. 10. 11. 12.

Chart 2.—Diminution in the discrepency between the percentage of complete protections in homes as compared to hospitals with increasing dosage of serum. In this chart *H* indicates hospital exposed cases; *F*, cases exposed at home.

per cent to 11 per cent. When dosages of from 12 to 25 cc. of adult serum were used for a group of children treated at home (column 4) of somewhat greater age range, from 2 to 12 years, but otherwise under similar conditions, there was a rise in the complete protections that were obtained from 46 per cent (with 8 cc. dosage) to 57 per cent.

Corroboration of these statistics may be deducted from the results reported by Morales and Mandry [3] (chart 2, columns 5, 6 and 7). They show a striking agreement with our results. With 10 cc. of adult serum they obtained 41 per cent against our 46 per cent with 8 cc. With 15 to 30 cc. they had 58 per cent protections against our 57 per cent with almost similar serum dosages. Morales and Mandry show 82 per cent protection with 30 cc. of adult serum and 85 per cent with 40 cc. of serum. When from 4 to 6 cc. of convalescent serum was used, they had 84 per cent protection.

Few reports have shown similar results in hospitals and homes, but only when convalescent serum has been employed in adequate dosage. Nabarro and Signy [4] (chart 2, columns 11 and 12) reported 97 per cent protected in hospitals and 94 per cent in homes when from 5 to 7 cc. of serum was used.

INFLUENCE OF HYGIENE

The fact that disease seems to spread more rapidly in congested districts and, above all, in those in which the hygiene is very poor suggested further analysis of our statistics with the hope of answering question 3; must we qualify our results according to the type of home in which the exposure takes place? If one considers a home of good hygiene in which the sick child is quickly isolated after the illness is discovered, and compares it to one in which the hygiene is poor (one in

TABLE 2.—*Diminution in the Discrepancy Between the Percentage of Complete Protections in Homes as Compared to Hospitals: with Increasing Dosage of Serum*

Author	Age	Exposure	Serum	Cases	Protected	Modified	Failed
Schick and Karelitz	2-10 yrs.	5 days or less	Hosp. A. S. 6 cc.	69	83%	17%	0
			Home 6 cc.	65	29%	22%	49%
			8 cc.	75	46%	43%	11%
			12-25 cc.	54	57%	20%	23%
Morales and Mandry	6 mos.-10 yrs. 50% less than 5 yrs.	6 days or less	Home A. S. 10 cc.	138	41%		
			15-30 cc.	321	58%	22%	20%
			30 cc.	34	82%		
			40 cc.	28	82%		
			Conval. serum 4-6 cc.	120	84%	11%	5%
Park and Freeman	.....	5 days or less	Conval. S.	652 Hosp.	91%	7%	2%
			Conval. S. 6 cc.	226 Home	52%	42%	6%
Levinson et al.	1-15 yrs.	5 days or less	3 cc. / 3 yrs. plus 0.5 cc. per 6 mos.	287 Home	60%	33%	7%
Nabarro and Signy	.....	.....	Conval. S. 5-7 cc.	461 Hosp.	97%	....	3%
			Conval. S.	125 Home	94%	....	6%

A. S., adult serum; Conval. S., convalescent serum.

TABLE 3.—*Results in 106 Cases of Infection under Standard Conditions Except for Exposure*

	Cases	Protected	Modified	Failed
Home hygiene good.....	32	58%	23%	19%
Home hygiene bad.....	26	0	27%	73%
Hospital.....	48	83%	17%	0

TABLE 4.—*Data of Attempt to Increase Existing Measles Immunity of Adults by Reinfection*

Author	Age, Years	Exposure, Days	Serum	Number Cases	Protected No.	Protected %	Modified No.	Modified %	Failed No.	Failed %
Schick and Karelitz	2-6	2-5	6 cc.	B 36	14	39	5	15	17	46
				A 38	23	63	11	26	4	11
				A_1 33	22	63	7	20	4	11
Schick and Karelitz: Hospital and home exposures	2-6	2-5	6 cc. Hosp.	B 8	6	75	2	25	0	0
				A 40	34	82	6	18	0	0
			6 cc. Home	B 28	8	28	3	11	17	61
				A 31	12	39	11	35	8	26
Schick and Karelitz: Donors M and R	2-10	2-5	8 cc. Home	B 35	14	40	17	49	4	11
				A 40	17	43	17	43	6	14

3. Morales, E. G., and Mandry, O. C.: Relative Prophylactic Value of Convalescent and Immune Adult Measles Serum, Am. J. Dis. Child. **39**: 1214 (June) 1930.

4. Nabarro, D. N., and Signy, A. G.: Convalescent Serum in the Prophylaxis of Measles, Brit. M. J. **1**: 12 (Jan. 3) 1931; **2**: 599 (Oct. 3) 1931.

which the sick and well children continue to be together after discovery of the illness), a striking difference in the results is demonstrable. Thus, if 106 children of from 2 to 6 years of age, exposed for from two to five days and injected with 6 cc. of serum, are divided into those exposed in homes of good hygiene, in those of bad hygiene and in the hospital, the percentages of completely protected cases are respectively 58, 0 and 83 (chart 3).

The difference in the results in homes of good and of bad hygiene is almost as striking as the results of patients treated with adult serum when tested in hospitals as compared to homes. In the home of poor hygiene the exposed child obtains the infection not only from one to five days before the serum is injected but throughout the period of infectivity of the sick sibling. Such a child may receive so great an infection that complete protection can be obtained only if a large dose of serum is given. This was apparently borne out by the fact that with increasing dosage of serum there was a progressively greater percentage of protected cases.

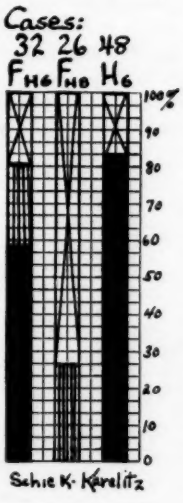

Chart 3.—Results in 106 cases of injection of serum under standard conditions except for exposure. F_{HG} indicates homes of good hygiene; F_{HB}, homes of bad hygiene, and H, hospital.

COMMENT

This influence of epidemiology in measles prophylaxis has been emphasized before. Jordon,[5] realizing that contact is much more intimate in home life than in hospitals, recommended larger doses of convalescent serum (from 6 to 18 cc.).

Park and Freeman, using 6 cc. of convalescent serum in institutions and at home, found striking differences in the percentage of children who were completely protected. The relation of hospital to home protection was 91/52.

Freeman and Freeman[6] stated that "in judging the results of a series of institutional children, the definiteness of exposure can never be accurately determined and it is safe to say that a good many of the children recorded as completely protected were never exposed."

The data of our 263 cases, when studied from the point of view of epidemiology, showed strikingly how different the results were with serum tested in the wards of hospitals or institutions as compared to familial exposures. The excellent results obtained in hospital wards were just as striking as were the poor results obtained in homes, under otherwise comparable conditions. Our results probably explain the high percentage of completely protected cases usually obtained with relatively small doses of serum when injected into susceptible children exposed to measles in schoolrooms, play groups, nurseries, asylums and especially children's hospitals.

Although it is true that, in such institutional epidemics of measles, all exposed susceptible children may develop the disease after the first exposure, it is far more common for only a few to come down with it after the first exposure and others after the second or third exposure. Under such circumstances it is doubtful whether a prophylactic procedure can be evaluated very accurately. It is safe to presume that in hospitals many of the so-called exposed children escaped infection entirely, while some may have been slightly infected and others infected intensively and repeatedly throughout the period of exposure. In pediatric institutions where there is a cubicle system or where isolation technic is observed, this difference in exposure must be evident.

A brief description of an experiment, a preliminary report of which has been published,[7] will serve to illustrate the importance of the epidemiologic factors pointed out in this paper. We undertook a study attempting to increase immune antisubstances of adults by reexposing them frequently and intimately to patients in the first few days of severe measles. Four volunteers were bled before, and eight and twenty-one days after the last of thirteen exposures to the disease of from thirty to sixty minutes. One hundred and eighty-two susceptible children exposed to measles for from two to five days were treated with serums of the four volunteers. Serum B refers to that obtained before reinfection, and A_8 and A_{21} to serums obtained eight and twenty-one days after the last exposure. The latter were so similar in their results that they will be generally considered together as A. The results with the serum of donors M, K, S and R are reported compositely and represented in columns 1 and 2 of chart 4. One hundred and seven children from 2 to 6 years of age who were exposed for from two to five days received 6 cc. of serum obtained from one of the four donors. Of the thirty-six injected with B serum, 39 per cent were completely protected, 15 per cent had modified measles and 46 per cent had unaltered measles. Of the seventy-one who received serum A, 63 per cent were protected, 26 per cent had modified measles and only 11 per cent developed ordinary measles.

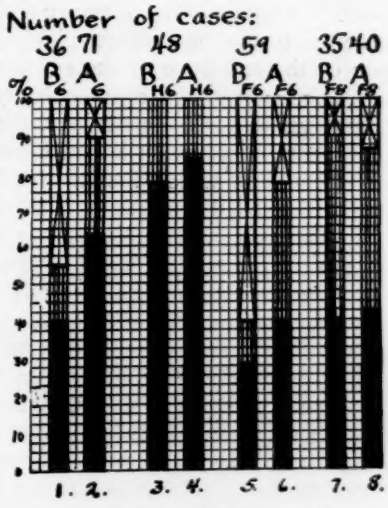

Chart 4.—Data of attempt to increase existing measles immunity of adults by reinfection. *B* indicates before reinfection; *A*, eight or twenty-one days after reinfection; H_8, patients injected with 6 cc. of serum in hospitals; F_8, patients injected with 8 cc. of serum in homes.

If these statistics are accepted at face value they indicate a marked increase of measles immunity following repeated reexposure to the disease. If, however, the epidemiologic factors discussed are applied to this study, the striking improvement that seemed to have been noted becomes much less evident, almost doubtful. Thus, if the 107 cases previously referred to are separated into hospital exposures and family exposures, we note that in the hospital group there were no failures in forty-eight cases, whereas the unprotected cases of the home (familial) exposures were numerous, twenty-five out

5. Jordon, H. P. B.: Measles Immunization, Rhode Island M. J. **9**: 71 (May) 1926.

6. Freeman, R. G., and Freeman, R. G., Jr.: Measles in Private Practice as Modified by Use of Immune Serum, Arch. Pediat. **43**: 563 (Sept.) 1926.

7. Karelitz, Samuel, and Schick, Bela: Masernschutzimpfung mit Erwachsenserum reaktiviert durch Exposition zu Masern, Wien. med. Wchnschr. **82**: 1395 (Nov. 5) 1932.

of fifty-nine, or 42 per cent. The difference between the percentage protected with serum A over that with serum B is thus greatly reduced. If, therefore, the conditions of the experiment were alike in all details except that the exposure to measles occurred at home rather than in the hospitals, we noted a striking difference in our results. The same observation was true for each donor studied, as demonstrated in chart 1. Furthermore, when the dosage of serum was increased from 6 to 8 cc. (chart 4, columns 7 and 8) and was tested in homes only, the number of completely protected cases increased but there was almost no difference in the results obtained with serums A and B. The latter experiment again demonstrates the necessity of considering the epidemiologic factors in studies of measles prophylaxis.

We believe that the evidence presented indicates clearly that the degree and frequency of repetition of exposure to measles within a few days determines in large measure whether the susceptible patients will develop the disease. In this respect it is not unlike tuberculosis and perhaps other infectious diseases.

The inadequacy of most hospitals and institutions for study of the prophylactic value of an antimeasles serum has been demonstrated. We would suggest that a serum may be declared effective only if it has been proved to be so after it has been tested under the severest conditions; namely, thorough and repeated exposure to sick siblings at home, or under comparable epidemiologic circumstances.

CONCLUSIONS

1. Hospital and institutional wards are usually inadequate for study of measles prophylaxis because of the uncertainty and difference of the intensity and duration of the exposure of the susceptible children.

2. The percentage of completely protected cases in homes varies with the hygiene, the greater number of protections being recorded in homes of better hygiene or in those in which facilities make possible isolation of the sick child at an early stage of the disease.

3. The percentage of complete protections in homes of poor hygiene increased progressively with corresponding increase of the serum dosage.

4. We believe that the evidence presented indicates rather clearly that the degree and frequency of infection with measles within a few days determines in large measure whether the disease will develop in the susceptible children. In this respect it is not unlike tuberculosis and other infectious diseases.

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Lengthening the Prime of Life.—It was coming to be thought that longevity was determined only by heredity, and that "while there are many ways in which you can shorten your life, the only way to lengthen it is by the selection of a longer-lived ancestry." We now know that this was a too fatalistic view and that, important as is the inheritance, the life cycle can also be extended by simple improvement of food habit such as is easily within individual and family control. And it is important to realize that this increased length of adult life induced by taking a larger proportion of the needed calories in the form of the protective foods means a longer prime of life, not merely a longer old age. The prime of life is in fact extended in considerably greater ratio than the life cycle as a whole; and it is extended in both directions, development being expedited and old age deferred in the same individuals by the same improvement in an already adequate food supply.—Sherman, H. C.: Food and Health, New York, Macmillian Company, 1934.

Clinical Notes, Suggestions and New Instruments

GRAPHIC METHOD OF INTERPRETING BLOOD VESSEL DISEASE OF THE LEGS: PRELIMINARY REPORT

BERTRAM M. BERNHEIM, M.D., BALTIMORE
From the Surgical Department of the Johns Hopkins Medical School.

When one sits with the legs crossed there is an almost invisible but natural swing of the foot that is synchronous with each heartbeat. If one attaches a short rod [1] to the side of the shoe of an individual sitting thus and lets the pointed tip of this rod rest lightly against the revolving drum of a sphygmograph, one will get a normal reading such as those in figures 1 to 5.

These graphs, as will be noted, show a dicrotic wave and correspond very closely to the sphygmogram tracings of the

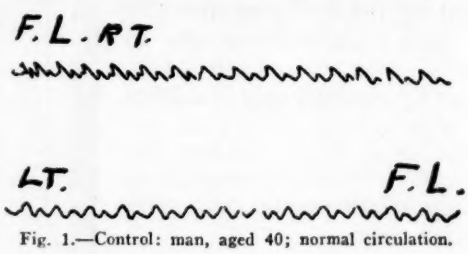

Fig. 1.—Control: man, aged 40; normal circulation.

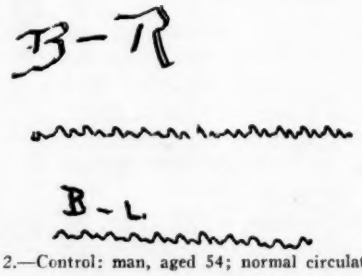

Fig. 2.—Control: man, aged 54; normal circulation.

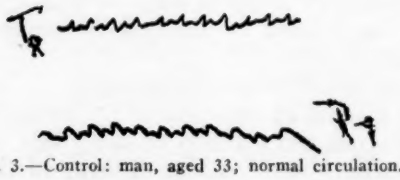

Fig. 3.—Control: man, aged 33; normal circulation.

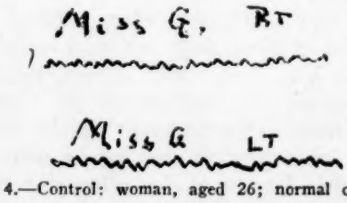

Fig. 4.—Control: woman, aged 26; normal circulation.

radial artery. There are slight variations, as one would expect, and many more control readings will have to be taken in order to get a clear idea as to just what they are and what they mean. They are being taken right along and there will be more to say on the matter later. Cardiac conditions and other factors must naturally be of some influence.

In making the tracings the one leg should be crossed over the other in such a way that the upper ends of the heavy calf

1. So far as the observations go—and of course this is subject to change—the length and character of the recording rod does not seem to be of great importance other than that the very tip should be fairly delicate and flexible. At present a rod is being used made of a light, narrow, rigid piece of wood 8 inches long to which by adhesive tape an ordinary thin strip of tin is attached, on the end of which, again by adhesive tape, there is attached a short piece of pointed x-ray film, the whole affair being about 11½ inches long. This contraption is attached to the inner side of the shoe at the sole by adhesive tape in such a manner that it projects about 6 inches beyond the tip of the shoe.

muscles rest on the patella. If the leg is crossed over too far the foot may have, and usually does have, a swing that gives a normal reading; but this swing is not as wide as is the case if the leg rests on the patella and consequently the peaks of the curve are not as high or as definite. Naturally, the individual should be as relaxed as possible and let the foot hang free. It is also best for him not to look at the drum as the tracing is being made.

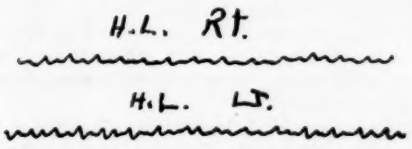

Fig. 5.—Control: boy, aged 13; normal circulation.

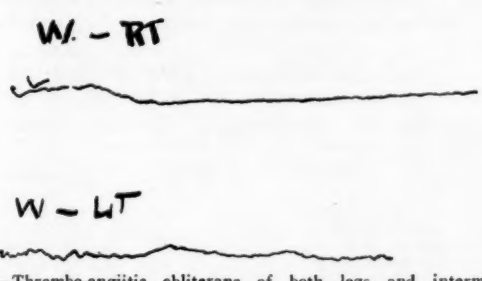

Fig. 6.—Thrombo-angiitis obliterans of both legs and intermittent claudication in S. W., a man, aged 33. Both femoral pulses felt. Both popliteals absent. No pulses in feet. The graph indicates that the patient has a very precarious collateral circulation. It is better in the left than in the right leg.

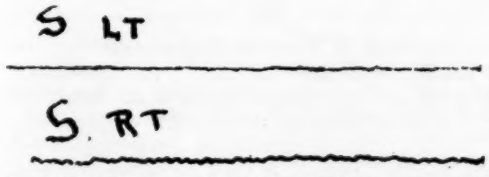

Fig. 7.—Thrombo-angiitis obliterans of both legs and intermittent claudication in S. S., a man, aged 39. Both femoral pulses felt. Left popliteal felt but no pulses in left foot. Right popliteal absent, right dorsalis pedis absent, right posterior tibial present. The collateral circulation is poor in the left leg and better in the right leg but not very good in either.

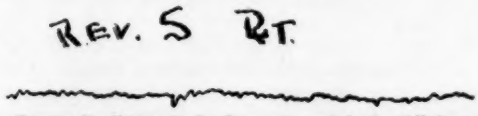

Fig. 8.—Raynaud's disease in L. S., a man, aged 33. All four extremities were involved. The left leg had been amputated. The popliteal pulse of the right leg was present but not good. No pulsation in dorsalis pedis. Questionable in posterior tibial. The patient had a fair circulation. Periarterial sympathectomy was done on the right leg four years before.

In the case of those who are suffering from blood vessel disease of the legs it has been found that the swing is much less than normal, even entirely absent, depending on whether the popliteal artery is partially or totally obliterated, and the status of the collateral circulation. It has further been found than many of these legs when crossed and placed for a reading have more or less of a tremor, very fine in some, rather gross in others, which gives an irregularity to the line of the graph. Certain normal individuals present a similar phenomenon, but it seems to be more commonly found in the diseased.

Before the test was tried on those with diseased blood vessels, it was felt that, if the popliteal artery was pulsating, a normal reading would be obtained; but this has proved to be far from true. Many patients whose popliteal artery can be felt—as in the case of Mr. G. D.—even well felt, present a very sad looking graph, so that the conclusion is reached that this test reveals very accurately the state of the leg's circulation, both natural and collateral. The less the swing, the more serious the condition; the greater the swing, the more positive and regular, the better the condition.

Curiously enough, though, no matter how good the circulation of a leg presenting vascular disease may be, the graph of that leg never seems to approach the normal with its dicrotic wave. Certain ones have suggested it but could not be considered truly normal, and one wonders whether a leg the normal blood channels of which have become obliterated can ever show such a thing. In every instance thus far in which a dicrotic wave has appeared constantly, palpation has revealed pulsating arteries in the entire leg and foot. Indeed, it would appear that—aneurysms possibly excepted and perhaps, to a certain extent, vasospasm—a plainly visible, regular foot swing indicates a normal circulation. One need not make tests, take graphs or palpate the vessels.

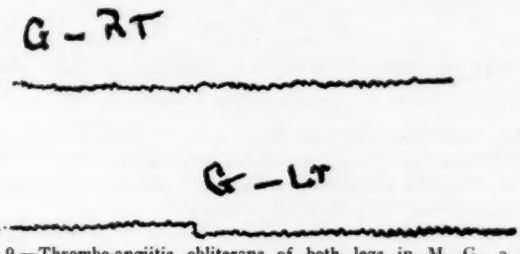

Fig. 9.—Thrombo-angiitis obliterans of both legs in M. G., a man, aged 37. Intermittent claudication. Ulcer on right big toe. Both popliteal pulses present but only fair. No pulses felt in either foot. Circulation fair.

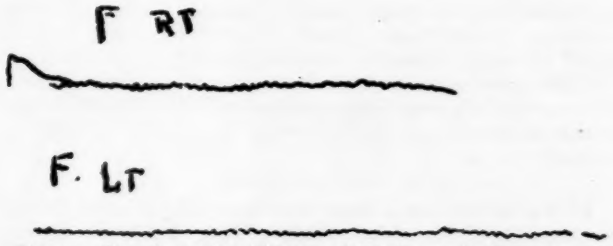

Fig. 10.—Thrombo-angiitis obliterans of both legs in S. F., a man, aged 31. Intermittent claudication. Neither popliteal pulse felt. Periarterial sympathectomy done on left leg (popliteal artery) seven years before. Collateral circulation is only fair.

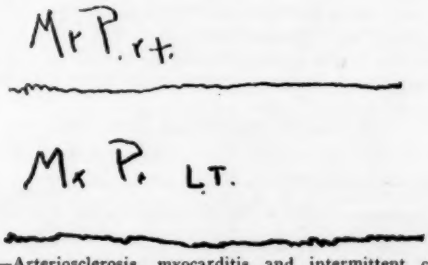

Fig. 11.—Arteriosclerosis, myocarditis and intermittent claudication, both legs, in D. P., a man, aged 61. Femoral pulses present in both legs. No other pulses. Collateral circulation precarious.

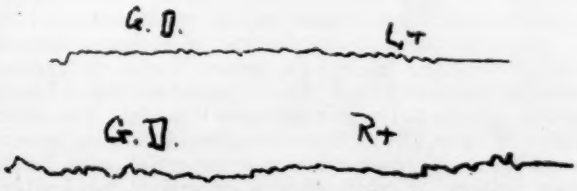

Fig. 12.—Arteriosclerosis and gangrene of left big toe, in G. D., a man, aged 70. Pain in the left leg. Threatened gangrene of the left foot. Intermittent claudication. Both femoral pulses felt. Both popliteal pulses are felt but the left is only fair. No pulses in either foot. Circulation poor in both legs, better in the right than in the left, which is the one affected. The patient was a thin man with blood pressure of 200 systolic, 95 diastolic, and the popliteal pulses were better felt than in any of the other cases reported, yet the graph shows that the circulation is anything but good, thus indicating that pulsation in the popliteal arteries is not necessarily a guide to the true state of the circulation below.

For the time being, opinion must be reserved as to the explanation of the phenomenon; but it has been suggested that it is due not to the pulsating popliteal artery itself but to the synchronous spread of the calf muscles consequent on the amount of blood sent to them.

It is thus apparent that here is a very simple and inexpensive method of graphically determining the state of the arterial circulation of the legs in both health and disease. And not only that, but by this method it will be possible by successive readings over a period of months or years to keep a pictorial record of such increase or decrease of the circulation as may take place.

This is a preliminary report and further work is in process, but it may be permissible to say that there are rather wide implications to this finding and much that is of interest awaits future studies. A further report will be made.

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HYPERSENSITIVENESS TO PITUITARY EXTRACT

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The continual increase in the administration of various biologic products by the several parenteral routes warrants an occasional word of caution with regard to the development of hypersensitiveness.

It is well known that this artificially produced hypersensitiveness is usually not of the strong, atopic type. Atopic hypersensitiveness may, however, under certain conditions, be produced artificially by injection. These conditions are for the most part unknown at the present time.[1] Hypersensitiveness of varying degrees results from injections of horse serum preparations. Sensitization to insulin is a well recognized condition.[2] Pituitary extracts, however, judging from reports in the literature, very rarely produce clinical hypersensitiveness. Hasson[3] in 1930 and Wang and Maxwell[4] in 1933 each report a case of general reaction following the injection of pituitary extract.

REPORT OF CASE

H. F., an American housewife, aged 28, in good general health, without personal or family history of allergic diseases, has had seven children. Following the birth of two of her first five children she was given a subcutaneous injection by her private physician (presumably pituitary extract). Her sixth baby was born in November 1933. Following delivery the usual subcutaneous injections of pituitary extract and ergot were given. There were no untoward symptoms following any of these injections. Her seventh child was born Nov. 8, 1934, and again the usual subcutaneous injections of pituitary and ergot were given. About thirty minutes later massive swelling

TABLE 1.—*Results of Skin Tests*

Pituitary extract (Obstetrical), Merrell	Strongly positive
Pituitrin (Obstetrical), P. D. & Co.	Strongly positive
Posterior Pituitary, B. W. & Co.	Strongly positive
Pituitary, whole, Armour	Slightly positive
Anterior Pituitary, B. W. & Co.	Negative
Pitressin, P. D. & Co.	Moderately positive
Pitocin, P. D. & Co.	Negative
Insulin, Squibb	Negative
Physiologic solution of sodium chloride	Negative

of the lips and face was noted and the patient complained that her tongue felt tremendously swollen. She began to have difficulty in breathing, which was evidently due to obstruction in the upper respiratory tract. The edema of the larynx increased rapidly and she had more respiratory difficulty. The administration of epinephrine relieved the situation and she recovered completely. The puerperium was uneventful until six days after delivery, at which time a generalized urticarial rash occurred with considerable itching and discomfort. This lasted five days and gradually subsided, leaving the patient feeling very well.

Skin tests on the patient, done by the scratch method, gave the results recorded in table 1.

The preparations listed in table 2 were made by emulsifying the fresh gland or other material in phenolized buffered saline solution (Alice Evans' solution). Tests were made by the scratch method.

Extracts of the following human tissues gave negative tests: pancreas, adrenal, liver, thyroid, spleen, brain (pons) and kidney.

Forty-five common foods, pollens, danders and other inhalants all gave negative tests. All tests, both positive and negative, were done in duplicate. All substances giving positive tests were applied in the same way to a normal person with negative results.

Skin tests done on the baby thirteen days after birth were entirely negative to the same pituitary extracts used in testing the mother.

Local passive transfer (Prausnitz-Kustner) with the patient's serum was strongly positive in each of the two recipients. The

TABLE 2.—*Tests with Various Preparations*

Pituitary, cattle	Strongly positive
Pituitary, hog	Strongly positive
Pituitary, human	Strongly positive
Cerebral cortex, cattle	Negative
Cerebral cortex, hog	Negative
Cerebral cortex, human	Negative
Skeletal muscle, cattle	Negative
Skeletal muscle, hog	Negative
Skeletal muscle, human	Negative

reaction in the prepared areas of these recipients could be elicited very well by the scratch method and also by the intradermal method. The controls were negative.

COMMENT

The development of a specific hypersensitiveness with local passive transfer of antibodies to the injected substance, pituitary extract, in a patient without personal or family history of allergy and with negative tests to the common allergens is worthy of note. This is particularly interesting in view of the fact that pituitary extract is used so extensively and allergic manifestations from it are reported so rarely.

No one particular brand is responsible, since positive skin tests were obtained with four different brands.

Pitressin, containing the vasoconstrictor principle, gave a positive test; but pitocin, containing the oxytoxic factor, gave a negative test.

The specificity is not directed toward some species specific factor distributed throughout the various tissues of some particular animal, or even toward the brain tissue of a particular species of animal. It is apparently directed toward some constituent of the posterior lobe of the pituitary gland of several animal species, including man himself. So far as I know this is the first recorded instance of a definitely established hypersensitiveness in man to a product of the human body. The late Bruno Bloch, for several years preceding his death, sought unsuccessfully to find a case of hypersensitiveness to a product of human metabolism.[5] Considerable theoretical importance attaches to this problem, since, if it could establish that a man could be sensitized to a product of his own body, it might offer a possible explanation for the existence of certain possibly allergic diseases which appear to be of intrinsic origin, such as certain types of asthma, eczema, urticaria and migraine.

In the case reported here, however, it is not established that the patient is sensitive to a product of her own body but merely that she is sensitive to a product of the body of some other human being, which may or may not be identical with the analogous product of her own body. It is well known that the tissues of one individual, skin for example, when grafted on the body of another person, seldom survive, while autogenous transplants are nearly always successful. It is obviously impossible to solve this problem in this particular case, since it is not possible to test this woman with an extract of her own pituitary gland.

Brown Building.

From the Department of Medicine, University of Louisville School of Medicine.

1. Coca, A. F.; Walzer, Matthew, and Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, 1931, p. 56.
2. Davidson, M. T.: Insulin Allergy, J. Allergy **6**: 71 (Nov.) 1934.
3. Hasson, James: Anaphylaxis Following Injection of Pituitary Extract, Brit. M. J. **1**: 242 (Feb. 8) 1930.
4. Wang, P. W., and Maxwell, J. P.: Protein Shock After the Administration of Pituitrin, Chinese M. J. **47**: 66 (Jan.) 1933.
5. Personal communication to the author. Schürch, O.: Reizversuche mit physiologischen Substanzen auf der Haut von Normalen und Ekzematikern, Klin. Wchnschr. **4**: 11 (Jan.) 1925. (Only eczematous hypersensitiveness studied by means of patch tests was investigated.)

SENSITIZATION PHENOMENA FOLLOWING THE USE OF SODIUM MORRHUATE FOR THE CHEMICAL OBLITERATION OF VARICOSE VEINS

LOUIS L. PRAVER, M.D., AND S. WILLIAM BECKER, M.D.,
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Untoward reaction in the form of a cutaneous eruption or a nitritoid crisis was observed in seven out of 176 patients who received 783 injections of 5 per cent sodium morrhuate (Searle) in the Dermatology Clinic for the chemical obliteration of varicose veins. Two patients received further sodium morrhuate injections without recurrence of the eruption, so the connection is not proved in these two instances.

The reactions were: urticarial eruption on the leg, two cases; urticarial eruption on leg and arm, one case; urticaria on arms, one case; pruritus, erythema and edema of arms, one case; pruritic erythematous eruption on leg, one case; weakness for two days, one case. Injections were continued in one patient with urticarial wheals at sites of previous injections, and a nitritoid crisis appeared after six injections, accompanied by cutaneous reaction only. The reaction seen most frequently consisted of grouped urticarial wheals at the sites of previous injections, which can be attributed with certainty to sensitization to sodium morrhuate.

EXPERIMENTAL WORK

The skin was tested with 5 per cent solution of sodium morrhuate: (1) by the scratch method; (2) by intracutaneous injection of 0.03 cc. (intradermal test), followed (3) in one week by a second intradermal injection of the same amount (for the Arthus phenomenon) and (4) in twenty-four hours by intravenous injection (for the Schwartzman phenomenon). Interpretation of results was difficult, owing to the irritating nature of the solution. The scratch test was interpreted as negative in nine patients and positive in two patients, both of whom showed signs of hypersensitiveness to the drug. Intradermal injection was made in twenty patients, with slightly increased reaction in most of the patients who were hypersensitive. The difference was not sufficient to be used as a guide. Repeated injection for the Arthus phenomenon was negative in ten cases. The Schwartzman reaction was not seen in fifteen cases; repeated attempts four and six weeks later in sensitive patients did not produce it. Passive transfer was attempted with the serum of one hypersensitive patient. Subsequent intradermal injection of 0.03 cc. of sodium morrhuate into the skin of the recipient at the site of the injection was followed by a reaction more marked than that following any intradermal test, so that it was interpreted as positive. In two other recipients of the same serum, subsequent application of sodium morrhuate by the scratch method produced no abnormal reaction.

Since the 5 per cent sodium morrhuate solution is irritating, it was diluted with sterile water and it was found that 0.03 cc. of a 1:640 dilution produced a visible wheal in a presumably nonsensitive patient. Further study is being made with diluted material. The solution was analyzed to determine the presence of protein and the total nitrogen content. The protein was too small in amount to be determined in a 20 cc. sample. Total nitrogen was 0.037 Gm. per liter. If one assumes that it is all protein nitrogen, the protein content would be 0.25 Gm. per liter, not enough to produce sensitization.

COMMENT

Cutaneous and nitritoid reactions followed the administration of sodium morrhuate in about 3 per cent of cases. Zimmermann reported similar reactions from the drug. He also emphasized the difficulty in interpreting cutaneous tests but suggests the performance of intracutaneous tests on a patient who has lapsed (presumably from ten to fourteen days) in order to determine the development of hypersensitiveness. The irritating nature of the solution suggests the advisability of using diluted material or other material, such as cod liver oil itself. This problem is being studied in this clinic. Animal experiments are being performed which may shed some light on the method of production of sensitization. The protein content is not sufficient in itself to produce sensitization, but the sodium morrhuate may act as a haptene and sensitize susceptible individuals. The eventual production of a nitritoid crisis in one of our patients emphasizes the desirability of changing to some other substance at the first sign of hypersensitiveness. It is also advisable, as stated by Zimmermann,[1] to begin with 0.5 cc. of sodium morrhuate for the first injection.

From the Section of Dermatology of the Department of Medicine of the University of Chicago. Read at the Scientific Session of the Section of Dermatology, Dec. 7, 1934.

1. Zimmermann, L. M.: Allergic-like Reactions from Sodium Morrhuate in Obliteration of Varicose Veins, J. A. M. A. **102**: 1216-1217 (April 14) 1934.

INSTRUMENTS TO FACILITATE THE INSTILLATION OF PROPHYLACTIC MEDICATION OF THE EYES OF THE NEW-BORN

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The occasional development of ophthalmia in the new-born is probably not due to the omission of the conventional prophylactic means employed but rather to faulty instillation of the bactericide instilled.

Fig. 1.—Instrument to facilitate the instillation of medication of the eyes of the new-born.

In order for the antiseptic solution used to be effective, it is essential that contact be made with all parts of the conjunctival sac. Simply, as so often occurs, to expose the membrane about the palpebral fissure is by no means sufficient. By the customary manual retraction of the eyelids, free and full exposure of the conjunctival membrane is rarely afforded.

By this method only partial exposure of the sac to the germicidal solution is as a rule attained.

Manual retraction, moreover, with the gloved fingers or the gloved fingers enveloped with gauze is more or less cumbersome and often proves inadequate in assuring that the antiseptic medication is properly instilled. By this method, furthermore, the antiseptic solution used may partially be absorbed by the gauze wrapped fingers, or, owing to the struggles of the infant, the material may simply fall on the lid margins and fail to reach thereby the important areas beyond.

In order to overcome the difficulties inherent in digital retraction of the eyelids of the new-born, the simple implements presented herewith have been designed.

One of us (Castallo) devised the instrument shown in figure 1. A description of this has appeared elsewhere.[1]

The implement shown in figure 2 is a modification of figure 1 and was designed by the senior author. In practice it is found to provide certain advantages. The small serrations on the edges of the blades of the instrument prevent slipping and, when properly placed in or rather under the orbital plates, owing to the special springlike action, it is more or less self retaining.

Fig. 2.—Modification of instrument.

The blades of both instruments are so shaped that, when placed over the closed eyelids and gently separated, the eyeball with the conjunctival sac is exposed without the slightest trauma. Hence, free instillation of the antiseptic solution is assured.

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From the Department of Obstetrics, Jefferson College Hospital.

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Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

ANTERIOR PITUITARY AND ANTERIOR PITUITARY-LIKE SUBSTANCES

THERAPEUTIC APPLICATIONS

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NOTE.—*This article and the articles in the previous issues of* THE JOURNAL *are part of a series published under the auspices of the Council on Pharmacy and Chemistry. Other articles will appear in succeeding issues of* THE JOURNAL. *When completed, this series will be published in book form.*—ED.

Up to a few years ago, efforts at anterior pituitary therapy were limited to the use of oral or hypodermic preparations, either of the anterior lobe alone or of the whole gland, in conditions of supposed deficiency, such as adiposogenital dystrophy, pituitary obesity or amenorrhea, dwarfism or infantilism. In this respect the common practice was almost analogous to the early methods of ovarian therapy in conditions of supposed ovarian hypofunction. Just as the clear differentiation of the ovarian hormones has completely changed the complexion of ovarian therapy, so have the recent advances in anterior pituitary hormonology changed the points of view and methods in pituitary organotherapy. The tendency now is to aim at hormone therapy rather than at mere gland treatment.

The important physiologic advances to which reference has been made have been fully reviewed in previous articles of this series. The present paper, like the one on estrogenic therapy, makes no pretense of being an exhaustive review, being offered rather as a brief summary and appraisal of the present status of the subject, and including only a minimum of references to the extensive and somewhat bewildering literature.

As a basis for the discussion of the therapy of the anterior lobe, the following hormones have been enumerated [1] as having their source in this structure:

1. The growth hormone, commonly accepted as being the product of the eosinophilic cells.
2. The gonadotropic hormone or hormones, generally believed to be formed by the basophilic cells.
3. The lactogenic hormone, shown by Riddle [2] to be the cause of lactation, but only when the mammary gland is previously subjected to the action of the estrogenic hormones.
4. The thyrotropic hormones on which the activity of the thyroid is dependent.
5. The fat metabolism hormone.
6. The blood sugar raising hormone.
7. The adrenotropic hormone.

Of all these, only the first two would seem, in the present state of knowledge, to merit any discussion from the standpoint of organotherapy. The lactogenic hormone (prolactin) may perhaps prove of clinical value as a galactogogue, but only one brief report,[3] based on a very small series of cases, has so far been made on this subject. Encouraging results are said to have been obtained.

CLINICAL CONDITIONS INVOLVING GROWTH HORMONE

Growth Abnormalities. — The best known of these, gigantism and acromegaly, are due to excessive production of the growth hormone, most often by adenomas of the acidophilic cells. Here the problem is not one of organotherapy but of correcting the endocrine excess by means of surgery or irradiation.

As types of deficiency of the growth hormone may be mentioned the growth deficiencies characterizing the various types of pituitary dwarfism and infantilism, especially the so-called Lorain-Levi and Brissaud types. While these are believed most often to be due to adenomas of the chromophobe cells, the obvious growth deficiency would seem to justify the use of preparations containing the growth hormone. Simmonds' disease [4] (cachexia hypophyseopriva), a rare disorder due to destructive disease of the entire anterior lobe, and characterized by emaciation, a prematurely senile appearance, amenorrhea and other symptoms, has in a few cases been treated by anterior pituitary preparations, either orally or hypodermically, but the results have not been striking.

Preparations Available.—No commercial preparation of the growth hormone has as yet been recognized by the Council on Pharmacy and Chemistry of the American Medical Association, which is not surprising in view of the present inability of manufacturers to prepare it in pure forms, and the meagerness and unconvincingness of clinical reports. In this country only three commercial preparations, so far as I know, are available; viz., the "Antuitrin G" of Parke, Davis & Co., the "Phyone" of the Wilson Laboratories and Anterior Pituitary Extract Squibb. These extracts all contain other active principles of the anterior pituitary in addition to the growth promoting factor. The more purified form of the growth hormone with which Evans has achieved such striking results in animals is not yet available commercially, although the manufacturers to whom it has been entrusted have been able to furnish small amounts for a few clinical and experimental studies. Engelbach [5] in 1930 reported satisfactory growth results in a pituitary dwarf of 9 years in whom treatment with the Evans purified growth hormone was carried out, with daily injections of the substance, for nine and a half years, 2.7 inches (7 cm.) in height being gained during this period. Engelbach and Schaefer [6] have recently reported encouraging results in seven cases of dwarfism. In these the growth hormone preparation (antuitrin G) was combined with thyroid, which Smith [7] has shown to increase the effect on skeletal growth. Both Evans and Reichert [8] emphasize the importance of having such growth hormone extracts free of gonadotropic principles, which might result in excitation of sex maturity, with epiphyseal closure and the cessation of growth.

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There are a few clinical reports by Cushing [9] and others of the use of preparations of the growth hormone in cases of pituitary growth deficiency, but, on the whole, the results have not been impressive. The chief hope for the future seems to lie in the preparation of the growth hormone in a purified form. If this is accomplished, there would be reason to expect far better results than those obtainable with the admittedly uncertain preparations now available. The recommended dosage of antuitrin G is 1 to 3 cc. two or three times a week.

CLINICAL CONDITIONS INVOLVING GONADOTROPIC HORMONES

An enormous impetus to anterior pituitary organotherapy was given by the discovery in 1926, by Smith and Engle in this country and Zondek and Aschheim in Germany, of the remarkable effects produced on the gonads of experimental animals by anterior pituitary implantations (see article on physiology of anterior pituitary, in this series). Because of the impracticability of implants for clinical use, and also because of the difficulty of preparing satisfactory extracts for clinical purposes, this discovery in itself would not have had much therapeutic significance had it not been for the further discovery by Zondek that the urine of pregnant women, even in the earliest phases of gestation, contains large quantities of "prolan," a substance believed by Zondek to be identical with the gonad-stimulating hormones produced by the anterior lobe. It is on the presence of this factor in early stages of pregnancy that the now universally employed pregnancy tests (Aschheim-Zondek, Friedman, Schneider, Brouha, and the like) are based, the principle producing in the sex glands of the injected animal changes that in most respects are similar to those produced by the pituitary hormones from the gland itself. As to the actual identity of the latter and the urinary factors, there has arisen much discussion, although this has no bearing on the reliability of the pregnancy test.

Likewise there has been much discussion as to the unity or the duality of the pituitary gonad stimulating principle. Zondek early differentiated two principles, one ("prolan A") having a follicle ripening effect and having to do with the production of estrogenic substance, while the other ("prolan B") is responsible for luteinization and the production of the corpus luteum factor, "progestin." There are many excellent investigators, however, who look on these two different effects as merely different phases in the activity of a single principle. This question, as well as that of the identity or lack of identity of the urinary and the pituitary gonad-stimulating hormones, has been discussed in a previous article and need not be elaborated on here.

The practical point is that anterior pituitary-like extracts made from the urine of pregnant women have been made available commercially and have achieved wide clinical vogue in disorders in which there is a supposed deficiency of the anterior pituitary gonadotropic hormones.

Preparations Available.—The chief American preparations of this type are the following: (1) "Antuitrin S" (Parke, Davis & Co.) prepared from the urine of pregnant women by a modification of the Zondek-Aschheim technic. It is put up in 10 cc. rubber diaphragm-capped vials, each cubic centimeter containing 100 rat units. The rat unit is described as the minimum quantity of hormone that will cause the formation of one or more corpora lutea within 96 to 100 hours when injected subcutaneously in six doses, twice daily for three days, into female white rats 30 days of age and taken from a colony the members of which become sexually mature normally in from fifty to sixty days. "Follutein" (Squibb) is described as a "sterile glycerin solution of the anterior pituitary-like gonadotropic hormone found in pregnancy urine." It is prepared from the latter by a technic essentially that described by Zondek and Aschheim. "It is then dissolved in glycerin, physiologically assayed, berkefelded and filled into 1 cc. syringe containers. Each cubic centimeter contains 1,250 rat units. Before administration the content of the syringe is added to 9 cc. of sterilized water, thus making 10 cc., each cubic centimeter having a potency of 125 rat units." The rat unit is described as "the minimum amount which, given in six injections on three consecutive days, produces mature follicles, hemorrhagic follicles and corpora lutea in the ovary within 100 hours after the first injection in 30-day old female rats."

It is quite possible that if the actual pituitary hormones, as obtained from the anterior lobe itself, are made available, they may prove to be much more effectual than the anterior pituitary-like principles of pregnancy urine now supplied commercially, for there seems to be much difference of opinion among investigators as to the exact source and nature of these principles, while their effect on the human ovary is certainly not what would be expected from the pituitary hormones themselves. One or two firms are now, I understand, engaged in efforts to produce the gonadotropic hormones from the gland itself, but there has as yet been no opportunity for worth while clinical investigation with them.

Functional Menorrhagia.—In this very frequent and very troublesome disorder, encountered at any age during the reproductive epoch, not infrequently during puberty or adolescence, and most often at or near the menopausal phase, clinical evidence indicates the definite value of therapy with anterior pituitary-like principle from the urine of pregnant women. This plan, suggested by Novak and Hurd [10] in 1931, was based on the fact that corpora lutea and progestin are lacking in this disorder and that there is presumably a lack of the luteinizing principle of the anterior lobe.

It was thought that the injection of a luteinizing principle obtainable from the urine of pregnant women would supply this deficiency. Since such a substance produces marked luteinization of the ovaries of mice and rats, it was even at first thought that the human follicle could be luteinized and progestin thus be produced, with a completion of the cycle and cessation of the bleeding. Opportunities to study the ovaries of patients who had received this substance have shown that the response is not at all similar to that of experimental animals and that luteinization is not produced. And yet the abnormal bleeding, in a large proportion of cases, is controlled. What the mechanism is one can only speculate, though it is obviously in some way dependent on the reciprocal functions of the anterior lobe and the ovaries.

The chief indication for such therapy is found in the cases of functional bleeding in younger women, in whom any form of radiotherapy is undesirable. In

9. Cushing, Harvey: Disorders of the Pituitary Gland, J. A. M. A. 76: 1821 (June 18) 1921.

10. Novak, Emil, and Hurd, G. B.: Am. J. Obst. & Gynec. 22: 501-512 (Oct.) 1931.

women approaching the menopause, once the diagnosis is established, radiotherapy is the method of choice, yielding success in practically 100 per cent of cases. In younger women and children, on the other hand, the frequent and often alarming recurrences of functional bleeding must be treated either by curettage, often repeatedly, or by organotherapy. Transfusion is not infrequently necessary.

No method of organotherapy yields as large a proportion of successes as follows the employment of the hypophyseal-like preparations, though there are many failures. Why the treatment is so strikingly successful in some cases and so unsatisfactory in others one cannot say, but certainly a proportion of the failures must be due to the uncertainties of the preparations used, for they are notoriously prone to deterioration, even with refrigeration. For this reason some clinics prefer to prepare their own material freshly from the urine of pregnant women, while some have utilized the serum of such women. Even the rectal infusion of the urine of pregnant women has been resorted to with apparent success.

When the commercial preparations are employed, as is commonly the case, a good plan is to withhold them until the onset of the bleeding, or, if this is not too free, until it can be determined whether it is actually to be abnormally long or profuse. Daily intramuscular injections are then begun, in doses of from 100 to 200 units, depending on the severity of the bleeding. In a few cases the hemostatic effect is remarkably prompt, bleeding being checked within a matter of hours. In others the injections may have to be given for four or five days, and the bleeding may be only markedly lessened instead of being checked entirely. In still others, as already stated, there may be little or no effect on the bleeding, so that other measures may be necessary. There is no objection to the plan of beginning the injections several days before the expected bleeding, although irregularity is so common in these cases that the patient cannot usually be sure of the date of onset.

Endocrinopathic Amenorrhea.—The anterior pituitary-like preparations (antuitrin S or follutein) are apparently of little or no value in the treatment of endocrinopathic amenorrhea, although, when combined with estrogenic substances (given either together or in sequence, the gonadotropic factor being administered last) they sometimes produce uterine bleeding (see paper on therapeutic applications of estrogenic substances). This method of ovarian therapy is usually combined with the administration of thyroid extract.

Adiposogenital Dystrophy (Fröhlich's syndrome).—This extremely common clinical picture with its adiposity of characteristic distribution (heavy girdle about the abdomen, hips and buttocks, large busts, shoulder pads) together with amenorrhea or scanty menstruation, undoubtedly has its chief source in a functional disturbance of the anterior lobe. Whether this may be a purely functional disorder or whether there is always present a chromophobic adenoma is a question that cannot be answered at the present time. Certainly there are many adenomas which, because of their small size and their position, cannot be demonstrated by any clinical or laboratory procedure at present. It seems certain, too, not only that in most cases of adiposogenital dystrophy, the gonadotropic hormones and the fat metabolism hormones of the anterior lobe are concerned but that the metabolic disturbance involves also, and perhaps chiefly, the immediately adjoining hypothalamic regions of the brain. This is indicated by the investigations of Smith and others.

The organotherapy of this condition is very unsatisfactory. The common plan utilizes various combinations of pituitary preparations, thyroid extracts, and ovarian preparations. The oral administration of pituitary preparations is looked on by most clinicians, and practically all laboratory investigators, as having no value. Other clinicians, however, employ these preparations quite extensively. Some, again, believe that while of no value in the usually advised dosage of 5 or 10 grains (0.32 or 0.65 Gm.) a day, they are effective in extremely large doses (from 60 to 100 grains [4 to 6.5 Gm.] daily). As the preparations are expensive, and as their use must be kept up for periods of many months and even years, this method would be prohibitive to most patients.

Thyroid therapy is probably of much greater value and may be used even when the basal metabolism is normal or only slightly subnormal, as is the usual rule. Comparatively small doses, for example 1½ or 2 grains (0.09 or 0.13 Gm.) of desiccated thyroid daily will usually suffice. When there is any noteworthy loss of weight from combined pituitary and thyroid therapy, it seems likely that it is the latter which is chiefly responsible.

As for the use of the anterior pituitary-like and the ovarian hormones in an effort to correct the amenorrhea and the genital hypoplasia, the indications and the results are not different from those pertaining to the treatment of endocrinopathic amenorrhea in general (see article on therapeutic applications of estrogenic substances).

Undescended Testicle.—An interesting clinical application of laboratory investigations is seen in the recent employment of the gonad stimulating preparations from the urine of pregnant women in the treatment of undescended testes. A scientific basis for this has been furnished by the observation by Engle,[11] in 1932, that the injection of these substances in immature monkeys brought about a descent of the testes, although this form of therapy had been employed before this (Shapiro, 1930). Goldman and Stern[12] have reported two cases of undescended testis, in which the use of injections of antuitrin S (100 units three times a week) was followed in a short time by descent of the gonads.

In a series of six boys suffering with the same condition, Sexton[13] obtained successful results in four. A very recent paper by Cohn[14] reports that similar treatment (with antuitrin S) was successful in five of six cases. In some of these, the descent of the testis seems to have occurred with amazing rapidity. For example, in a boy of 11 the undescended right gonad, previously palpable at about the middle of the inguinal canal, "descended six hours after the injection of anterior pituitary-like substance and remained well down after four months." Finally, reference may be made to the very recent study by Aberle and Jenkins[15] of the effects of this form of organotherapy in both human beings and monkeys. In two of four boys receiving the treatment the testes descended, but in

11. Engle, E. T.: Endocrinology **16**: 506-512, 513-520 (Sept.-Oct.) 1932.
12. Goldman, A., and Stern, A.: New York State J. Med. **33**: 1095 (Sept. 15) 1933.
13. Sexton, D. L.: Endocrinology **18**: 47-58 (Jan.-Feb.) 1934.
14. Cohn, Samuel: Anterior Pituitary-Like Principle in the Treatment of Maldescent of the Testicle, J. A. M. A. **103**: 103-104 (July 14) 1933.
15. Aberle, S. B. D., and Jenkins, R. H.: Undescended Testes in Man and Rhesus Monkeys, J. A. M. A. **103**: 314-318 (Aug. 4) 1934.

only one was the descent complete. In immature monkeys complete descent occurred in one animal and only partial descent in four, although Engle had obtained complete descent in eight of ten monkeys.

In view of the frequent failure of surgery to correct this condition, the endocrine treatment, as outlined, would seem to be indicated in cases of undescended testis before operation is resorted to, although a far larger experience with the method is necessary before one can draw conclusions as to its degree of dependability. The recent report by Geschickter, Lewis and Hartman [16] that the anterior pituitary-like gonadotropic factor produced hypertrophy of the prostate in a monkey to a degree that urethral obstruction resulted, indicates the necessity for caution in the clinical use of this principle.

Other Indications.—Habitual abortion, which often presents a baffling problem, has not infrequently been treated with the anterior pituitary-like factor, in the form of ether antuitrin S or follutein. The cause of this condition cannot in many cases be determined, and it is believed that some at least are due to a deficiency of the corpus luteum secretion so important for implantation and for the maintenance of fixation of the ovum in the early stages of pregnancy. Since no active preparation of the corpus luteum hormone (progestin) is available, it is not surprising that the pregnancy urine preparations have been employed as the next most rational means of treating this condition. Failures are common, though they are not usually reported. On the other hand, some successes have been reported, and the treatment seems a justifiable one to employ, but more needs to be known of the underlying cause or causes of this condition.

Primary dysmenorrhea, another *bête noire* of gynecologists, is a disorder of protean etiology. Many causes have been advanced and the methods of treatment suggested have been legion. The psychogenic factor is unquestionably the important one in many cases, the constitutional one in others, while in still others it seems probable that an endocrine imbalance may be concerned. No gynecologic disorder, therefore, makes greater demands on the knowledge, thoroughness and common sense of the gynecologist. A summary of the general plan of treatment is given elsewhere.[17]

The physiologic investigations of Reynolds [17] and many others indicate that, just as estrogenic substance is the natural stimulant of the normal rhythmic uterine contractility, so progestin and the anterior pituitary-like principle contained in pregnancy urine are inhibitors of this contractility. This fact, together with the fact that the immediate factor in the pain of primary dysmenorrhea seems to be a spasmodic contraction of the uterine musculature, has led to the suggestion that a part of the treatment in some cases—but only a part—should consist of the administration of antuitrin S or follutein beginning several days before the onset of the painful periods.

The dose suggested is from 100 to 200 units each day until the first or second day of the flow, after which most patients ordinarily suffer little pain with or without treatment. Because of the ever-present psychic factor which must be considered in the evaluation of results in such a subjective disorder, it is difficult to appraise the effect of this addition to the therapeutic armamentarium. At times the results seem brilliant, in other cases only improvement without disappearance of the pain is reported by the patient, and in still others the results are disappointing. However, in the treatment of a disorder in which there is so much therapeutic floundering as in that of primary dysmenorrhea, the plan suggested is worthy of trial, especially as it is far more rational than most others which have been suggested. It should again be emphasized, however, that in all cases of this group there should be a comprehensive survey of the constitutional, pelvic, psychic and even sociologic status of the patient.

In 1933 Brosius and Schaefer [18] reported a case of complete aspermia in which the intramuscular injection of antuitrin S (2 cc. twice a week) was followed by spermatogenesis, so that at the end of nine weeks numerous motile spermatozoa were found in the semen, while the testes showed a definite increase in size. Needless to say, this observation, interesting as it is, needs confirmation through trial in a large number of cases. In two recent cases of sterility in my practice in which the responsible factor was the husband's aspermia, the method suggested here failed to produce spermatogenesis.

In 1931 Bengtson [19] reported striking results in sixteen cases of alopecia treated by anterior pituitary substance. He recommended the hypodermic use of a pituitary gland preparation as preferable to the oral route, although the combination of the two methods gave the most rapid response. While he considered that all these cases belong to the category of glandular alopecias, he suggested that possibly other common types of baldness might also respond to the treatment. In spite of the author's own conservatism in this regard, the paper was taken up rather sensationally by the daily press. There has been no confirmation of his observations, and Lord [20] and others have reported unsuccessful results from the method. There seems to be no reason to expect benefit from it except perhaps in cases of genuine hypopituitarism in which the alopecia is a part of the general picture. Even here the usual limitations and uncertainties of pituitary therapy would prevail.

SUMMARY

The employment of the growth hormone preparations is indicated in the various types of pituitary growth deficiency. The results are usually not striking and will probably not be improved until biochemists isolate the hormone and produce more potent preparations.

The anterior pituitary-like preparations are probably of no value when used alone in the treatment of amenorrhea, and even when combined with estrogenic substance the results are very little improved.

The anterior pituitary-like preparations made from pregnancy urine have appeared to give excellent results in many, though not by any means all, cases of functional uterine bleeding, so that, when this disorder is encountered in young women, in whom radiotherapy is undesirable, the method should certainly be tried.

The comparatively small group of cases thus far reported in which undescended testis has been successfully treated by the anterior pituitary-like preparations make this method seem promising and worthy of more

16. Geschickter, C. F.; Lewis, Dean, and Hartman, C. G.: Am. J. Cancer **21**: 828 (Aug.) 1934.
17. Novak, Emil: Am. J. M. Sc. **175**: 237-244 (Feb.) 1933. Novak, Emil, and Reynolds, S. R. M.: The Cause of Primary Dysmenorrhea, J. A. M. A. **99**: 1466-1472 (Oct. 29) 1932.
18. Brosius, W. L., and Schaefer, R. L.: Spermatogenesis Following Therapy with the Gonad Stimulating Extract from the Urine of Pregnancy, J. A. M. A. **101**: 1227 (Oct. 14) 1933.
19. Bengtson, B. N.: Pituitary Therapy of Alopecia, J. A. M. A. **97**: 1355 (Nov. 7) 1931; Clin. Med. & Surg. **41**: 76, 1934.
20. Lord, L. W.: Anterior Lobe Pituitary Extract in the Treatment of Alopecia, Arch. Dermat. & Syph. **28**: 381-383 (Sept.) 1933.

extended trial, especially as the surgical treatment of this condition is not as satisfactory as might be wished.

There is no objection to a trial of the anterior pituitary-like preparations in the occasional mysterious and baffling cases of habitual abortion, although the results are not much more clearly defined than is the etiology of the condition.

These preparations appear rational as adjuvants in the treatment of primary dysmenorrhea, although correction of constitutional and psychic factors is often much more important, and should never be overlooked.

As to other conditions, such as aspermia and baldness, the clinical data thus far available are much too meager to draw conclusions as to the results of treatment with the anterior pituitary-like preparations, and there are physiologic reasons to make one question the value of this plan.

It is possible that the results of organotherapy in various forms of anterior hypopituitarism may be improved with preparations of the gonad stimulating hormones obtained from the anterior lobe itself.[21]

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Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE. HOWARD A. CARTER, Secretary.

AIDS IN MUSCLE TRAINING

WITH SPECIAL REFERENCE TO SLING SUSPENSION AND UNDERWATER EXERCISES

F. J. GAENSLEN, M.D.
MILWAUKEE

Of the many varieties of physical therapy, active exercise probably deserves first place because of its wide applicability and because it calls into play the entire neuromuscular units in a manner approaching normal physiologic action.

SLING SUSPENSION EXERCISES

Some ten years ago I described the "sling suspension" method of exercise as an aid in restoration of muscle power in infantile paralysis. The method has been employed for this condition ever since and has also been found useful in many other conditions. Briefly, the method consists in supporting the arm or leg to be treated in a sling suspended from overhead, thus eliminating the weight of the extremity as a hindrance during movement. The adaptability to the upper and lower extremities, as well as the fact that the method can readily be taught to nurse or mother, makes further mention of the method worth while. These exercises are helpful in allowing the patient to translate even minimal and scarcely appreciable muscle power into

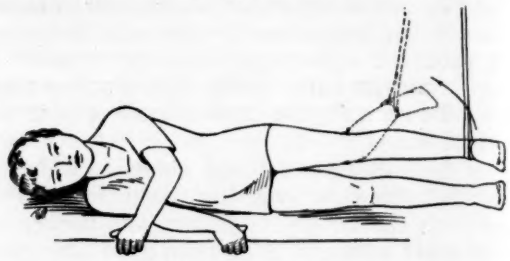

Fig. 1.—Sling about ankle to allow flexion and extension at the knee, the hip being fixed in extension by patient or instructor. With an additional sling about the knee, and releasing the fixation at the hip, the patient may execute movements in flexion and extension of the hip and knee simultaneously.

active and readily demonstrable motion through a fair arc. The fact that even slight gains are recognized by the increase in range of motion is of great importance in spurring on the instructor and the patient to continued efforts in the long and tedious process of restoration of muscle power.

The method is so simple that it can be employed to advantage in the case of even very young children. Resistance may be added, as indicated, in carrying out the exercises.

It is well at the outset to have the power of the muscles, or muscle groups, of the upper and lower extremities charted, the values being roughly estimated on the basis of 100 per cent, or listed respectively as normal, good, fair, poor, trace and zero, so that on comparison, at suitable intervals, some information may be obtained as to the rate of progress or perhaps cessation of progress.

If, after a period of gradual improvement, the condition remains stationary for a period of six months or more, it is reasonable to assume that no further noteworthy improvement is likely. Continuance of efforts under such conditions is not likely to be rewarded with marked benefit.

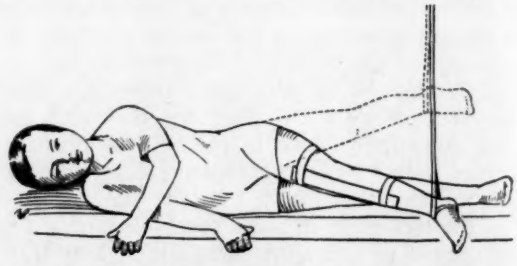

Fig. 2.—Patient on the side to allow flexion and extension at the hip, the knee being splinted to prevent buckling.

After it has been determined which muscles are to be exercised, the mother or attendant is instructed in the proper arrangement of the slings and overhead supports, and in carrying out the exercises as prescribed for the individual patient. The physician, or physical therapy technician, if one is available, should have no difficulty in a few short interviews and demonstrations

21. Following are additional references relating to this subject:
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Futcher, T. B.: Internat. Clin. **4**: 114-141 (Dec.) 1933.
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in teaching the mother or nurse the maneuvers necessary in the particular case. Occasional checking and supervision of exercises by the physician are desirable.

In the average case of infantile paralysis, because of the long duration of treatment, it is not practicable to have the child brought to institutions daily or several times daily for treatment by skilled physical therapy technicians. Neither is it practicable to have the skilled workers visit the children in their homes as often as treatment is indicated. The solution for the case of this type lies in the enlistment of the services of some one in the household, usually the mother. Exercise periods, for the most part, should be brief to avoid fatigue, but they may be, and usually should be, repeated frequently during the day, with proper rest periods intervening. The mother therefore is the one logical person to carry this out. I have found that the average lay mother requires but a few practical lessons in order to acquaint her with the relatively small number of special procedures applicable in the case at hand. She can be taught to carry this out fairly satisfactorily, even though she does not understand the physiologic

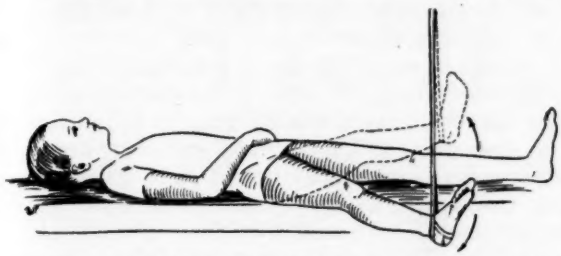

Fig. 3.—Sling about ankle to allow abduction and adduction at the hip.

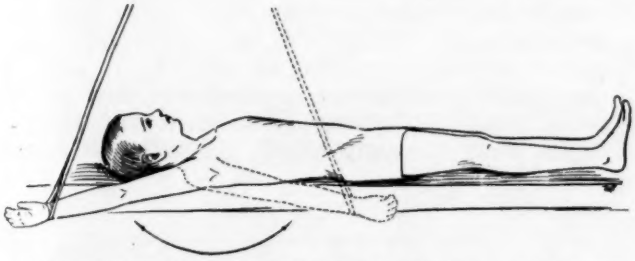

Fig. 4.—Patient lying supine with the sling about the wrist, allowing abduction and adduction at the shoulder.

principles involved. Such a program, of course, requires occasional supervision and correction of errors, and also modification from time to time.

In the case of the lower extremity the use of the roller skate, ball-bearing device attached to a shoe has been found an advantage in facilitating early motion. This contrivance has been found very helpful in fractures of the lower extremity. With the ball-bearing under the heel and the lift under the knee, regulated by the patient himself, the gentlest movements in flexion and extension can be executed, just as much assistance being given as the case may require and without danger of injury, if ordinary care is used. Resistance in the shape of push and pull by the mother or attendant may be added. This arrangement provides for flexion and extension of both knee and hip as well as for abduction and adduction of the hip. Abduction and adduction are provided for by turning the wheels, fixed to the shoe, at right angles. This type of exercise will be found useful in practically all types of fracture of the lower extremity, including especially fracture of the patella and fracture of the neck of the femur where special care is indicated. There is probably little doubt that some potentially good results, after fracture of the neck of the femur, are ruined by too early removal of apparatus in bed. The strain at the fracture site, from the constant tendency of the thigh and foot to rotate out, represents a force that probably results frequently in a gradual giving way of the soft callus, with the result of a fibrous union. The directions to move the leg in bed in the sense of abduction and adduction, or, worse still, to try to lift the heel from the bed with the knee extended, cause tremendous force to come into play, which tends to angulate the neck into a position of coxa vara. In a leg slightly edematous, still greater caution is indicated because of increased weight. This internal stress on the bone, due to muscle pull, is very considerable, as Carey has demonstrated. It is more than likely that attention to details of this character would help cut down the percentage of failure in fractures of the neck of the femur, and to reduce the healing period in this as well as other fractures of the lower extremity.

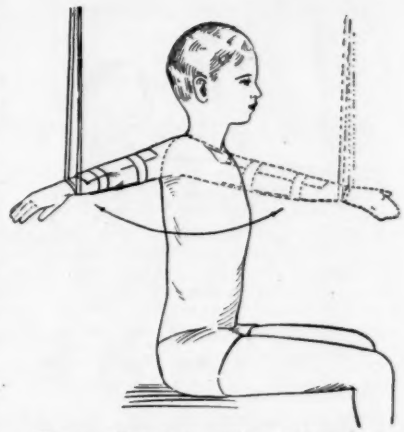

Fig. 5.—Patient in sitting posture with sling about the wrist, the elbow being splinted to prevent motion at this joint; the arm may be swung forward and backward from the shoulder.

Other conditions in which sling suspension may be employed with benefit include spastic paralysis, especially of the lower extremities, and atrophic arthritis, as well as in cases of weakness and stiffness after fracture or injury. In spastic paralysis it has frequently been found of advantage to attach a heavy weight to the sling, transforming it essentially into a pendulum with heavy weight. The patient's arm or leg is placed in the sling and the pendulum is put into motion by the instructor, the patient being taught to continue the swinging with and without resistance. It is felt that a good start may be made in this manner in developing the sense of rhythm and in the teaching of gentle coordinate movement.

Fig 6. — Patient seated with arm at the side, the wrist again supported with the sling to allow rotation movements at the shoulder.

In arthritis, active motion within the pain-free range is without doubt a factor of considerable importance in the maintenance of normal physiologic joint activity. The alternate contraction and relaxation of muscle groups and their antagonists must be of help in improving the circulation. As the muscles contract, the lymph vessels and veins are compressed, the blood and lymph being hurried in the proximal direction. As the muscles relax, these vessels are filled from the capillary side, the capillary system in turn drawing on the arterial supply. In this manner capillary stasis is overcome, and definite acceleration of the blood stream results.

All the tissues of the part, including those of the joint, are benefited by the improved circulation. Cell growth, repair and defense, as well as elimination, are enhanced. It is felt that the use of the ball-bearing apparatus in atrophic arthritis is of special value, since, with the apparatus in place, the patient can exercise frequently for brief periods, always in the pain-free range. Practically all the joints of the lower extremity, and those of the upper extremity as well, are brought into play, the latter through the rope and pulley hand control.

Fig. 7.—Patient seated with arm abducted to horizontal level, the sling supporting the wrist, allowing flexion and extension of the elbow.

UNDERWATER EXERCISES

Of perhaps equal importance as an aid in muscle training are underwater exercises. While suitable for infantile and other types of paralysis, atrophic arthritis, and weakness and stiffness of the extremities after injury, this type of exercise will be found useful as well in many instances in the field of internal medicine, neurology and psychiatry.

The advantages of underwater exercises are that (1) the buoyancy of water eliminates gravity and (2) the warmth of the water relaxes the muscles and accelerates the blood flow. The steady, gentle resistance of the water is readily overcome even by feeble muscles. The degree of resistance varies with the speed of motion.

The large pools, indoor and outdoor, are used mostly in the treatment of infantile paralysis and spastic paralysis. The most desirable temperature for infantile paralysis is about 91 F. For spastic cases a slightly higher temperature, about 95, is desirable to produce greater relaxation. It is doubtful whether the great sacrifices, financial and otherwise, made in many instances to provide pool treatment are justified by the results. The ordinary tub or small home-made tank in the average home will answer very well except in unusual cases. They have the advantage that the temperature can be regulated to suit the individual and that the water is renewed for each bath.

While the best results can probably be obtained by specially trained instructors, it is believed that the physician or competent physical therapy technician can teach a mother or attendant the necessary exercises in the individual case with a minimum of expense and with results that will probably compare very favorably with treatment in the large pool.

I have found the so-called Hubbard tub,[1] which is finding favor in many hospitals, of great help. I would be loath to do without this important part of physical therapy equipment. Such a tub installed in a room in a general hospital will be found very helpful in all cases in which wide abduction movements of the arms or legs are very desirable.

OVERHEAD TROLLEY SYSTEM

By means of an overhead pulley, the patient is gently hoisted on a hammock from the bed and carried by trolley to a position directly over the tub, and then gently lowered into the water. Underwater massage and active and passive exercises, as well as resistance exercises, are then readily administered according to the needs of the individual case. Aside from the facilitation of motion due to the warmth and buoyancy of the water, nervousness is allayed and patients frequently drop off after the bath into a sound sleep. The need for narcotics is diminished and the patient is spurred on to increased effort by the realization that definite and rapid progress is being made.

Caution must be exercised to avoid fatigue both general and local. There is perhaps a natural tendency to err in this respect, because it is more or less of a chore to get a patient into the pool or tub and, when the patient is once in the water, both patient and instructor are apt to overstep safe limits. No general rules can be laid down. Careful observation of the patient while in the tub as well as the first few hours following will be necessary to detect evidence of fatigue.

In infantile cases, muscles will often be found to show signs of fatigue after four or five efforts; therefore, frequent rest periods are indicated. In cases of injury it will rarely be advisable to keep the patient in the tub more than twenty or thirty minutes. Special care should be exercised also to prevent chilling. Warm blankets and towels should be in readiness after removal from the tub to avoid this danger. It is felt that both sling suspension and underwater exercises are of particular value, because they permit early active function. This ranks first along physical therapeutic measures because it calls for function of the neuromuscular unit as a whole. This unit is composed of the motor cell in the brain cortex sending its axon down the pyramidal tract to make contact with the lower motor neuron in the spinal cord. The axon of the latter in turn makes contact with the contracting muscle cell. In addition, the inhibitory mechanism is called into play, so that finely graduated precise movements are possible. Again, every voluntary muscle contraction is accompanied by a corresponding relaxation of antagonistic muscles. The voluntary effort automatically calls into play every portion of this complicated mechanism, which cannot be claimed for other agencies.

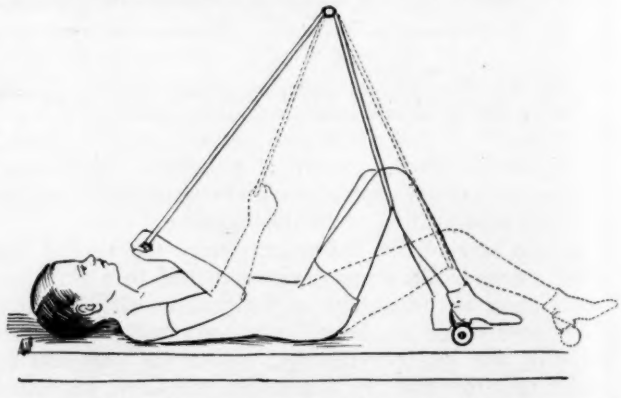

Fig. 8.—Sling under the knee suspended from a pulley attached to an overhead bar and controlled by the patient. The roller attached to the heel may be rotated through 90 degrees. A large piece of beaver-board may be placed on the bed to provide a smooth surface.

While the beneficial effects of such simple exercises for normal as well as injured parts are readily appreciable to the patient, as well as to the physician and attendants, and presumably attributable to improvement of circulation, it is desirable to have some scientific explanation for this improvement. Moving pictures of

1. Blount, W. P.: A New Hydrotherapy Tub, J. Bone & Joint Surg. **10**: 506 (July) 1928.

the circulation in the rabbit's ear and the effect of a rise of surrounding temperature on the circulation, prepared by Drs. Eliot R. Clark and E. A. Swenson of the anatomy department of the University of Pennsylvania, are of interest in this connection. These show that, while at ordinary temperature the circulation through the capillaries is slow, one may say sluggish, a moderate rise in temperature is accompanied by a very marked increase in the rate of flow. That exercise exerts a similar influence is indicated graphically in the charts prepared at the Mayo Clinic, based on the work of Goldschmidt and Light. These show that the number of open capillaries in a given area of skin surface is more than doubled by exercise and that heat also increases their number, while cold decreases their number in marked degree. In this connection, too, the work of Wright and Marquardt is of interest. They studied the capillaries in the nail bed of the finger and found that while in a normal, active individual the

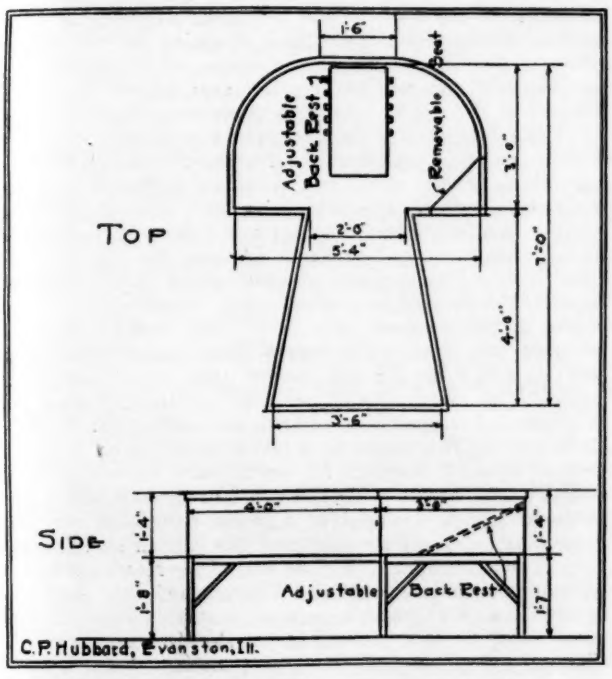

Fig. 9.—A plan of tub with dimensions. From Blount, N. P.: J. Bone & Joint Surg. **10**: 506-508 (July) 1928.

capillaries were rather closely packed in hairpin-like loops, those of the crippled arthritic hand were much less numerous and narrower, indicating that the little used, crippled hand was receiving a minimum of blood.

One is too apt to think of physical therapy in connection with injuries when, as a matter of fact, there is a large field for this branch of therapy in internal medicine, neurology and general surgery as well as in the specialties. I recall visiting the clinic of Professor Bardenheuer in Cologne in 1912. He had all his fracture cases in one large ward and made it a rule that when he entered the ward the patients immediately started carrying out certain exercises, not for the fractured limbs which may have been encumbered by splints or plaster casts, but for the uninjured limbs for the purpose of keeping up their general muscle tone and nutrition as well as the function of the heart and lungs.

One is also still too apt to forget that the body as a whole suffers with the injury of the part and that attention to these self-evident facts will do much to shorten convalescence and reduce the economic burden incidental to invalidism. There is little danger, except in infantile paralysis, of the patient overtaxing his strength during recumbency, because he can interrupt the exercises on the slightest signs of fatigue and resume them after suitable rest periods.

It must be emphasized that every case, of whatever type, must be studied carefully and a physical therapeutic program mapped out to meet the individual requirements, and also that the simple measures outlined here are merely aids in the rehabilitation program.

425 East Wisconsin Avenue.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. THE COUNCIL'S CONSIDERATION OF BAYER ASPIRIN WAS BEGUN PREVIOUS TO THE HEARINGS OF THE FEDERAL TRADE COMMISSION IN THIS MATTER AND COMPLETED WITHOUT KNOWLEDGE OF THE CONTENT OF THE COMMISSION'S PUBLISHED DECISION. THIS REPORT REPRESENTS THE COUNCIL'S INDEPENDENT ACTION AND WAS NOT INFLUENCED BY THE GOVERNMENT'S ACTION.

PAUL NICHOLAS LEECH, Secretary.

THE PRESENT STATUS OF ASPIRIN-BAYER

Aspirin-Bayer was omitted from New and Nonofficial Remedies in 1917 because of objectionable lay advertising of the product. The attention of the Council on Pharmacy and Chemistry was again called recently to the present character of the lay advertising promulgated by the manufacturers of Bayer Aspirin. An inquiry was received from the National Better Business Bureau, Inc., asking information as to the validity of the claims for curative value in colds made in this advertising. In the interest of the public, the Council therefore made a new survey of the advertising for Bayer Aspirin and found it more flagrant and insidious than that for which the product was long ago omitted from New and Nonofficial Remedies.

During the past decade, but more particularly within the past five years, Bayer Aspirin has been the subject of extensive lay promotion by advertising in newspapers, in periodicals and by radio. A wide variety of therapeutic claims has been made, ranging from mere statements of alleged superior solubility to outright and unqualified claims for actual prophylaxis and cure of the common cold. A number of claims, intermediary to these two extremes, relating to the relief of aches and pains of indiscriminate anatomic distribution also occur. Likewise may be found many statements pertaining to the alleged endorsement by the medical profession of Bayer Aspirin in preference to other brands; to absolute safety in the use of the product irrespective of dosage; to its harmlessness on the heart (with the implication that such harmlessness is characteristic only of the Bayer preparation), and to its alleged greater rapidity of action. Probably no better idea concerning the general nature of the advertising can be conveyed than by the presentation of a number of selected and oft repeated quotations which have appeared in one or another newspaper or periodical from 1929 until the present:

"See These Pictures If You Take Aspirin. They Show Why Genuine BAYER ASPIRIN is Rated the Fastest Safe Relief From Pain. . . . the *fastest safe relief, it is said, ever known for pain.*"—Chicago *Tribune*, Oct. 13, 1933.

"It's safe in anybody's hands; it has no ill effects. It always helps; it never harms."—Chicago *Herald and Examiner*, Feb. 10, 1929.

"Buy the genuine. Bayer Aspirin is made carefully. It has the endorsement of the medical profession."—New York *Sunday News* (date not stated).

"They don't depress the heart, and may be taken freely. That is medical opinion. It is a fact established by the last twenty years of medical practice."—New York *Sun*, Oct. 15, 1931.

"Take some Bayer Aspirin. Take enough to bring complete relief. Genuine aspirin can't hurt anybody. . . . They aren't just for headaches or colds! Read the proven directions covering a dozen other uses; neuritis; sciatica; lumbago; muscular pains."—New York *World Telegram*, Oct. 15, 1931.

"Any doctor will tell you they are harmless. They don't hurt the heart. They don't upset the stomach. So take them as often as you have the least need of their quick comfort."—*Collier's* magazine, Feb. 27, 1932.

"Bayer Aspirin does not depress the heart."—Chicago *Tribune*, April 28, 1931.

"Take two or three tablets when you've caught a cold, and that's usually the end of it. . . . From a grumbling tooth to those rheumatic pains which seem almost to bend the bones, Bayer Aspirin is ready with its quick relief. . . . *Any* nagging, needless pain."—Chicago *Tribune*, May 5, 1932.

"Take Bayer Aspirin at the first sign of a cold and you can ward it off."—(Reference unknown but clipping on file.)

"You can head-off a headache by taking these tablets, or nip a cold in the bud. . . . But read the proven directions, and be ready to end more serious suffering."—Los Angeles *Times*, Nov. 8, 1931.

"If you have a cold—don't take chances with 'cold killers' and nostrums. A cold is too dangerous to take chances on. The simple method pictured above [reference to picture of a man taking one or two Bayer Aspirin tablets with a full glass of water] is the way doctors throughout the world now treat colds. It is recognized as the QUICKEST, safest, surest way. For it will check an ordinary cold almost as fast as you caught it. That is because the real BAYER Aspirin embodies certain medical qualities that strike at the base of a cold almost INSTANTLY. . . . If throat is sore, gargle with 3 BAYER Aspirin Tablets crushed and dissolved in a half glass of warm water, repeating every 2 or 3 hours as necessary, Sore throat eases this way in a few minutes, incredible as this may seem. Ask your doctor about this."—Chicago *Tribune*, Nov. 11, 1932.

Bayer Aspirin has been actively promoted from coast to coast in a variety of publications as an utterly harmless sedative for symptomatic mitigation in a variety of conditions, and as a specific remedy for the prevention, abortion or cure of the common cold. Many other questionable statements might have been cited, but a critical discussion of those just quoted should suffice to illustrate their general unreliability. It should first be pointed out that Bayer Aspirin is merely a commercial proprietary name for the U. S. P. acetylsalicylic acid (from which it differs solely by its extensive advertising to the laity). For this reason it is classified in the general group of coal-tar antipyretics, which group, by reason of the similar therapeutic properties of its constituents, is useful in alleviating certain of the symptoms attendant upon the common cold. It has been contended that a threatening cold may be "aborted" by compounds of this group before it has become fully established; but to prove this it would be necessary to compare adequate series of threatening colds, one given the drug and the other not. No report of such a study can be found. Though the fever, headache and malaise may be minimized, there is no reason to believe that the usual course or duration of the common cold is in any way altered by the administration of acetylsalicylic acid of any manufacture. Physicians use these coal-tar antipyretics for the alleviation of symptoms of colds; not in any sense as a cure. Few, if any, competent physicians would subscribe to the claim, express or implied, that Bayer Aspirin, or any chemically identical or similar substance, is a specific remedy for colds and sore throats, or that it will cure such disorders.

The following claims are more explicity considered:

Concerning greater solubility: Though it may be true that tablets of Bayer Aspirin disintegrate more quickly in a tumbler of water than do some other brands, there still is no evidence to show it any more rapid in the production of its effect in the patient. Regardless of the consistency of the original preparation, the drug must pass into the intestine before absorption in therapeutic quantity can take place, and the time ordinarily required for passage from stomach to intestine would probably be ample to allow of the disintegration of practically any preparation of acetylsalicylic acid, so that rapid disintegration of a tablet on contact with water does not appear pharmacologically significant.

Concerning medical endorsement: Here the burden of proof properly devolves on the firm. In 1917 (at about the time the patent expired on Aspirin) when the firm decided to adopt frank "patent medicine" methods in promoting the product, the Council published its first adverse report, omitting the product from New and Nonofficial Remedies. Since that time, THE JOURNAL has, on a number of occasions, commented adversely on the product.

Concerning use as a gargle: The claim that "sore throat" is eased in a few minutes by gargling with a solution of Bayer's Aspirin, three tablets in half a glass of warm water, has not been proved by convincing evidence. Some observations indicate that the warm water is as effective as the Aspirin.

Claim of harmlessness: The claims thus far discussed, though unfounded, do not embody any serious direct menace to individual or public health such as is unquestionably involved in the statements concerning the absolute harmlessness of Bayer Aspirin. Acetylsalicylic acid may be and has been repeatedly shown to be potentially harmful, directly or indirectly, when taken indiscriminately. Indirectly, its use may mask symptoms which, instead of being those of an approaching cold, a simple headache or a mild lumbago, might represent the prodromal stages of an acute infectious disease, pneumonia, brain tumor, brain abscess, tuberculosis, cancer of the spine, or any number of serious diseases too numerous for specific citation. It is only too obvious that an inestimable amount of harm will be done by treating an early pneumonia with aspirin until too late, or maltreating scarlet fever until the delay has inaugurated a community epidemic. It is quite true that it would be unpractical, even if it were desirable, that people should "run to the doctor," every time that they are a little out of sorts, or think that they are. It is the physician's function to instruct his patients as to what they individually may with reasonable safety undertake in the way of self treatment, adapting the advice to the common sense, intelligence, education and temperament of the individual. It is not safe, either for the individual or for the public, to rely on advertisements for this instruction.

There is also the possibility of direct harm to the individual from the drug itself. On this score a number of reports of serious reactions appear in the literature. Mann[1] reports a case of myocardial impairment secondary to aspirin poisoning. Kraus[2] as early as 1914 reported a series of cases exhibiting allergic manifestations (urticaria; acute edema, either local or general; erythema, and pruritus) following the ingestion of as little as from 5 to 10 grains of acetylsalicylic acid. Roch[3] has reported the production of some gastric irritation. Block[4] has shown the toxic effects in animals to be identical with those of other salicylates, while Hanzlik[5] has demonstrated acetylsalicylic acid to be one and one-fifth times as toxic as sodium salicylate in man. Stiell[6] recorded chronic poisoning with symptoms of conjunctival catarrh and urticaria following a daily dose of 20 grains over a period of six years. The most serious reported reactions in recent years were observed by Lamson and Thomas.[7] They record four cases of severe sensitivity to aspirin contained in a patent asthma powder. One patient died in acute air hunger within half an hour following the self administration of but one half of the recommended dose. The three other cases exhibited a prompt induction, or marked aggravation of asthmatic symptoms, requiring epinephrine for relief. One of these patients was rendered unconscious by the reaction and required the constant attendance of her physician for several hours thereafter. These authors conclude that "an abnormal response to acetylsalicylic acid is probably more common than to any other drug." The paucity of reports in the literature would not appear to substantiate such a conclusion. It is certain, however, that there are many more such instances which do not find their way into print and that there is always the possibility of injury to the individual. The fact that abnormal response is uncommon provides no solace for the victim, who has been assured of the absolute harmlessness of aspirin of any brand.

Finally, it should be emphasized that practically all American brands of acetylsalicylic acid are of pharmacopeial standard, to which all legally sold products must conform. The claims that there exist radical differences between Bayer Aspirin and other brands of acetylsalicylic acid manufactured by reputable concerns are unsubstantiated. Actually, the only impurity likely to occur in any reputable brand is salicylic acid (in mere traces only), which is of identical action and of no practical significance whatever as a contaminant.

1. Mann, W.: Secondary Impairment of Cardiac Muscle Caused by Aspirin Poisoning, Med. Klin. **29:** 85 (Jan. 13) 1933.
2. Kraus, A. D.: Aspirin, Arch. Dermat. **119:** 1, 1914.
3. Roch, M.: Salicyl, Bull. gén. de thérap. **163:** 218, 1912.
4. Block: Salicyl, Inaug. Diss., Giessen, 1909.
5. Hanzlik, P. J.: A Study of the Toxicity of the Salicylates Based on Clinical Statistics, J. A. M. A. **60:** 957 (March 29) 1913.
6. Stiell, W. F.: Chronic Aspirinism, Practitioner **99:** 293 (Sept.) 1917.
7. Lamson, R. W., and Thomas, Roy: Some Untoward Effects of Acetylsalicylic Acid, J. A. M. A. **99:** 107 (July 9) 1932.

The Council has authorized the publication of this report and has confirmed its rejection of Bayer Aspirin for inclusion in New and Nonofficial Remedies because:

1. The unrestrained advertising of the Bayer product has given it an unfair advantage over other brands the manufacturers of which have adhered to the code which the Council has established in the interest of public health.

2. It is expected that this unfair advantage will be reduced in the degree that the misleading advertising of Bayer Aspirin is restricted.

3. The indiscriminate use of Bayer Aspirin, as urged in the advertising, is inimical to public and individual health, both directly and indirectly.

4. Aspirin (acetylsalicylic acid) is potentially a dangerous drug and its unqualified use as a home remedy should be undertaken, originally in any case, under the guidance of the family physician, whose knowledge of the personal characteristics of the individual patient can alone render such use safe and advisable.

MENINGOCOCCUS ANTITOXIN

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

A review of recent studies convinced the Council that meningococcus antitoxin shows a promise that makes it worthy of more extended clinical trial; the evidence, however, not being sufficient to warrant unlimited acceptance, the Council voted to accept the product submitted by Parke, Davis & Co. for one year only, in the hope that this acceptance may result in a clearer evaluation of its usefulness. At the end of that period the Council will give the product further consideration. A general description of meningococcus antitoxin, with a description of the accepted brand, appears in the New and Nonofficial Remedies Department of this issue.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

MENINGOCOCCUS ANTITOXIN.—An antitoxin prepared by the immunization of animals to polyvalent filtrates of six to eight day hormone-broth cultures of the four Gordon groups of meningococcus, after the method of Ferry, Norton and Steele.

Actions and Uses.—The published studies on the effect of the antitoxin in experimental meningococcic septicemia in guinea-pigs and rabbits, in experimental meningomyelitis in monkeys and in clinical epidemic meningitis in man suggest (1) that the symptomatology of the disease is attributable at least in part to the effects of a toxin produced by the organism and (2) that the clinical manifestations of the disease, its commoner complications and its mortality rate may all be favorably affected by the timely and proper administration of the antitoxin. The antitoxin should be used only in specific infections with the meningococcus, and the usual precautions concerning the administration of horse serum should be observed.

Dosage.—Dependent on the condition of the patient, the degree of toxemia and the occurrence of complications, from five to ten thousand units of antitoxin may be administered intraspinally, intracisternally or intravenously, at twelve to twenty-four hour intervals. The usual case is said to require a total of from 50,000 to 100,000 units.

Parke, Davis & Co., Detroit.

Meningococcus Antitoxin-P. D. & Co.—An antitoxic serum prepared by immunizing horses to bacteria-free meningococcus toxin, preserved with 0.3 per cent of tricresol. The antitoxin is standardized by human skin tests, the skin test dose of meningococcus toxin being that which when injected intradermally into a susceptible individual will produce a local skin reaction at least 10 mm. in diameter. The unit of meningococcus antitoxin is ten times that amount of the antitoxin which, when mixed with one skin test dose of meningococcus toxin, will produce a negative reaction or a reaction appreciably less than 10 mm. in diameter, provided the controlled toxin reaction is appreciably more than 10 mm. in diameter. The final product is standardized to contain not less than 350 units of meningococcus antitoxin per cubic centimeter. It is marketed in packages of one vial having a diaphragm stopper at each end and containing 10 thousand units of antitoxin.

Committee on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

ARROW BRAND SWEETENED CONDENSED MILK
LION BRAND PURE SWEETENED CONDENSED MILK
NESTLE'S BRAND SWEETENED CONDENSED MILK
SILVER BRAND SWEETENED CONDENSED MILK

Manufacturer.—Nestle's Milk Products, Inc., New York and San Francisco.

Description.—Sweetened condensed milk prepared from milk and sucrose.

Manufacture.—Fresh milk from dairies under the company's supervision is strained, cooled and delivered to the condenseries in clean cans and tested for cleanliness, freshness and flavor. The milk is standardized as to fat and solids content, heated to 85 C. and sucrose is added. The mixture is held at 85-90 C. for five minutes, is concentrated in a vacuum pan at 55 C. to somewhat less than one third of its original volume to conform to the United States Department of Agriculture standard for sweetened condensed milk, cooled to 18 C., and sealed in cans.

Analysis (submitted by manufacturer).—	per cent
Moisture	26.0-27.0
Total solids	73.0-74.0
Ash	1.7- 1.8
Milk-fat	8.0- 8.1
Protein (N × 6.38)	7.6- 8.2
Sucrose	44.0-45.0
Lactose	11.0-11.9
Carbohydrates (by difference)	56.7-54.9

Calories.—3.3 per gram; 94 per ounce.

Claims of Manufacturer.—Conforms to U. S. Department of Agriculture definition and standard for sweetened condensed milk.

WARRANTY SIEVED PEACHES

Manufacturer.—The Nielsen Corporation, Ltd., Oakland, Calif.

Description.—Sieved peaches prepared by efficient methods for retention in high degree of the natural mineral and vitamin values. No added sugar or salt.

Manufacture.—Fresh peaches are pitted by hand, passed through a lye peeling machine to remove skins, thoroughly washed to remove any adhering lye, and sorted to separate fully ripe from slightly underripe fruit. The former is either sieved immediately, as in the case of Warranty Sieved Spinach (THE JOURNAL, Feb. 2, 1935, p. 399), or canned and used later as needed for sieving.

Analysis (submitted by manufacturer).—	per cent
Moisture	87.4
Total solids	12.6
Ash	0.6
Sodium chloride	trace
Fat (ether extract)	0.2
Protein (N × 6.25)	0.5
Reducing sugars as invert sugar	3.4
Sucrose	4.7
Crude fiber	0.6
Carbohydrates other than crude fiber (by difference)	10.0
Titratable acidity as malic acid	0.7

Calories.—0.4 per gram; 11 per ounce.

Vitamins.—The method of preparation and processing insures the retention in high degree of the natural vitamin values.

Claims of Manufacturer.—Specially intended for infants, children and convalescents, and for special smooth diets. Only warming is required for serving.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, MARCH 23, 1935

VARIATIONS IN BEHAVIOR OF VITAMIN D

In 1919 Huldschinsky announced his observations on the efficacy of artificial ultraviolet irradiation in rickets. Four years later, Goldblatt and Soames demonstrated that irradiation of rats resulted in the development of antirachitic potency in the livers of these animals. The next year both Hess and Steenbock showed that when many food materials are exposed to these short wavelengths they exhibit antirachitic potency. In the course of the search for an explanation of the antirachitic activation, it has been demonstrated that the potency always follows the nonsaponifiable fraction of the lipids, that the activated material is rather resistant to ordinary laboratory manipulation, and that overirradiation results in the destruction of the effective compound. Naturally attempts were made to activate crystalline cholesterol; it is rendered highly potent by exposure to ultraviolet rays and retains this potency after a great many recrystallizations. Because activated cholesterol lost its potency when subjected to bromination and subsequent regeneration, it was concluded that a contaminant of cholesterol was responsible for the response to ultraviolet rays. Through studies based on fractional crystallization and on the absorption spectrums, ergosterol was identified as an accompaniment of cholesterol and was shown to be subject to intense activation by ultraviolet rays.

Once the fact was established that ergosterol is a precursor of vitamin D, there were reported many experimental studies which demonstrated the enormous potency of irradiated ergosterol solutions when compared to other recognized antirachitic substances such as cod liver oil and egg yolk. These comparisons were based on the official biologic assay in which the healing of the epiphysis of the femurs of rachitic rats is taken as the criterion of efficacy. After a time it was observed that, in tests of the toxicity of irradiated ergosterol, chickens were extremely resistant to overdoses of this material. When a comparison of viosterol (irradiated ergosterol) dissolved in oil with cod liver oil was made on the basis of the prevention of leg weakness in chickens, the latter was enormously more effective. Addition of vitamin A to viosterol failed to increase its efficacy in preventing leg weakness in chicks. The same superiority of cod liver oil over viosterol and irradiated yeast was demonstrated when the proportion of ash in the leg bones of chickens was the criterion. Russell, Taylor and Wilcox[1] have recently shown that a higher percentage of bone ash and superior egg production were secured with cod liver oil than with many times the number of "rat units" of vitamin D given in viosterol but that superior storage of this vitamin resulted in liver and egg yolk when viosterol was employed. Again, rats were used in assaying the organs. A still more striking instance of discrepancy between these two widely used sources of the antirachitic factor has been cited by Bills, Massengale and Imboden.[2] They compared cod liver oil with about 100 units per gram with blue fin tuna liver oil with 40,000 units per gram (both oils assayed with rats) on the basis of the behavior in chicks; the blue fin tuna oil was only a sixth as effective as was the cod liver oil.

Similar comparisons between the various sources of vitamin D have been made in cases of human rickets. The question has become particularly pertinent with respect to milk that has been enriched in the antirachitic factor by various methods. Earlier studies indicated a discrepancy in the results with infants between cod liver oil and viosterol when the two were fed in amounts containing the same number of "rat units," the former, as with chickens, being more effective. More recent investigations of activated milks indicate that milk irradiated directly is superior to cod liver oil when fed in amounts providing the same number of "rat units." One suggestion for the enhanced antirachitic value of irradiated milk attributes peculiar efficacy to the protein-sterol combination that has been demonstrated in milk.[3]

There is accumulating a mass of experimental evidence which, when correlated, will inevitably result in a change in current views regarding the interrelationships between the various dietary factors providing what is now called vitamin D. It is evident that man, the chick and the rat each exhibits what appears to be a specific quantitative response (but which really may be a qualitative one) to various sources of vitamin D. It has been suggested that the antirachitic factors from different sources are not identical.[4] Furthermore, the view that ergosterol is the provitamin D of cholesterol has been challenged recently by Waddell,[5] who has presented evidence indicating that, when irradiated, cholesterol itself, apart

1. Russell, W. C.; Taylor, M. W., and Wilcox, D. E.: J. Biol. Chem. **107**: 735 (Dec.) 1934.
2. Bills, C. E.; Massengale, O. N., and Imboden, Miriam: Science **80**: 596 (Dec. 21) 1934.
3. Sterols in Milk, editorial, J. A. M. A. **103**: 190 (July 21) 1934.
4. Steenbock, Harry; Kletzien, S. W. F., and Halpin, J. G.: J. Biol. Chem. **97**: 249, 1932.
5. Waddell, J.: J. Biol. Chem. **105**: 711 (July) 1934.

from the contaminating ergosterol, is rendered active in curing rickets. As inevitably happens, examination in closer detail of a collection of apparently well integrated circumstances has brought out some disturbing contradictions. However, this is part of the greater sweep of progress.

ASPIRIN-BAYER

Elsewhere in this issue (p. 1005) the Council on Pharmacy and Chemistry publishes a report on "The Present Status of Aspirin-Bayer." The methods employed by the exploiters of this brand of acetylsalicylic acid make desirable a recapitulation of the history of this product.

The original home of Aspirin-Bayer was Germany. Neither that country nor any others of importance would grant a patent either on the product acetylsalicylic acid or on the process of making it. The United States patent office granted both. As a result, for seventeen years—the life of a patent—it was impossible for any one in our country to manufacture or sell acetylsalicylic acid except the Bayer Company. Neither was it legal to import the substance. The monopoly thus granted the Bayer concern under the patent made it possible for the company to exploit the American medical profession and the public by charging an exorbitant price for aspirin.

More than twenty years ago THE JOURNAL collected data from American consuls abroad regarding the price at which acetylsalicylic acid was sold in foreign countries. At the time, American druggists were paying 43 cents an ounce for aspirin. The American public was, of course, paying still more for it. During the same period acetylsalicylic acid was being sold to druggists in France, Germany, Holland, Denmark, Sweden and other countries in continental Europe for 4 cents an ounce, and in Great Britain for 6 cents an ounce. The American had to pay nearly eleven times as much for his acetylsalicylic acid as did the citizens of most other civilized countries.

In February 1917 the patents on aspirin expired. Then the company that had reaped the benefit of its monopoly attempted to continue the monopoly by claiming it had the exclusive right to the use of the trademark "Aspirin" under which the public had purchased the Bayer brand of acetylsalicylic acid. Fortunately the courts would not sustain this claim. Any pharmaceutical house may now manufacture acetylsalicylic acid and sell it under the name aspirin.

There followed a period during which the Bayer concern carried on an advertising campaign which led the public to believe that the only "genuine aspirin" on the American market was the Bayer product. The same campaign also stressed the alleged harmlessness of Aspirin-Bayer. As the company, like most of those employed in the "patent medicine" business, was shrewd enough to take advantage of the weakness of the present national Food and Drugs Act, which cannot control claims made elsewhere than on or in the trade package, it was not possible to reach the concern through the Food and Drug Administration. In June of last year, however, the Federal Trade Commission served a complaint against Bayer Co., Inc., of New York City, charging misrepresentation in the sale of aspirin tablets. The company was given until July 13, 1934, to file its answer, showing cause why the commission should not issue an order requiring it to cease and desist from the practices complained of.

The company, through its counsel, filed an answer asking that a hearing on the charges be waived and consenting to the commission serving an order to cease and desist. The commission thereupon ordered the company to cease and desist from representing in newspaper and magazine advertising or over the radio that aspirin is the trademark of the Bayer brand of acetylsalicylic acid and from making such claims as

> "It does not depress the heart."
> "It cannot harm the heart."
> "Bayer aspirin is always safe."
> "Perfectly harmless."
> "You could take it every day without harm."

and many other similarly false and misleading claims. It was also ordered to cease claiming or representing that aspirin not made by the Bayer company is spurious or counterfeit.

This order was issued in September 1934. In the interim between the serving of the complaint and the issuing of the cease and desist order the Bayer Company brought down the retail price of its aspirin tablets to a price more nearly comparable with competing brands. It thus appears that exorbitant prices were first and foremost based on the monopoly granted through the patent law and, secondly, that an artificial price level was maintained by means of misleading claims to superiority together with the unjustified charges against its competitors.

IS THERE A "MORAL CENTER" IN THE BRAIN?

The cerebral localization of some peripheral actions is well established. The localization of others is merely a matter of speculation and debate; thus the status of sleep and heat regulation is still uncertain. When applied to more complicated phenomena such as the so-called moral sense, evidence for or against a "center" is even more difficult to assess.

Yawger [1] has recently discussed the possibility of a "moral center" in the brain based on the dissociation of social morality and certain intellectual or artistic qualities. Among the "idiot savants," he says, was "Blind Tom," a Negro musician of great talent. He was born a slave, and when he was 7 years old the family of his master, hearing strange music, found him

1. Yawger, N. S.: Is There a "Moral Center" in the Brain? Am. J. M. Sc. **189**: 265 (Feb.) 1935.

at the piano. He could at once reproduce the tunes he heard and repeat them after long intervals. Some of his music was from the classics and, if it had been played nervously when first heard, that too was included in the rendering. He could play a different tune with each hand at the same time, yet he was so foolish he would rise and, with his audience, applaud his own accomplishments. His intelligence was about that of a child of 4 years. There is room here for a reasonable doubt as to what quality might be localized.

Yawger refers also to Jesse Pomeroy, whose criminal career began at 13 with crimes of an especially brutal character. Pomeroy spent about forty years in solitary confinement, yet he read extensively, studied law and acquired some knowledge of several languages. Wainewright, another noted criminal, had an artistic temperament and was a poet, art critic, antiquarian and prose writer as well as a gifted forger and as subtle and secret a poisoner as has been known in almost any age. His known murders were numerous, but there were probably many that never received judicial notice.

Gilles de Rais, the original of Bluebeard, serves as another illustration of the combination of exceptional intellectual with exceptional criminal attainments. He could speak three languages and manifested great interest in military matters. His crimes were atrocious—apparently mostly of a sadistic type—and it was proved that he kidnapped or enticed to his castle at least 140 children.

Through disease, injury and shock, the mind may be strangely affected. There are many instances on record of persons whose intellectual characters have been markedly altered by such traumatisms.

This evidence as to a "moral center" in the brain is unconvincing. If "morality" is a purely human trait, however, there can be no other source of evidence than by observation of human behavior. Moral sense is more closely allied to emotion than to intellect. The frequent dissociation of emotion and intellect may be nothing more than the alternating control of action by the lower and higher nervous centers.

Current Comment

TRACK ATHLETICS AND MUSCLE PHYSIOLOGY

Records in track athletics have gradually improved, notwithstanding the fact that men predicted twenty years ago that the height of ability had been reached. The human mind is ingenious. Improvements in style of running and in training have permitted records to be lowered again and again. Previous to 1888 it was customary for runners to start standing up. In that year a Yale athlete, C. H. Cherrill, first used the crouching start. He won his race and since that time almost all sprinters have used the crouch in their start. It is said that the starting blocks were invented by Bresnahan, the track coach of Iowa. These were originally designed to keep athletes from digging holes in the track for their feet. A study of their value, however, indicates that they permit a faster start because of their firmness, the average advantage being about one foot. Coaches are still working for ways of permitting athletes to start faster. According to Thomas K. Cureton they are now working on some system of ropes or grip handles that will permit the runner to stand in the running position, or really to get a running start while standing still. Some studies made by Japanese and recently confirmed by American investigators show that the amount of time runners are held in position while crouching ready to start is important. The fastest start is secured when they are held in this position one and a half seconds. The Iowa coach showed that left-handed athletes should start with the right foot, and right-handed athletes with their left foot forward. The best sprinters take a long breath and hold it just after the command "Get set." Holding the breath allows them to focus their attention better and perhaps aids the drive from the legs through fixing the abdominal muscles. The extensive studies that have been made indicate how science is able to help the runner in improving his speed. It is important for runners not to start cold. A famous record holder found that he started fastest in the sixth to the ninth start when twenty starts were made in a row. The investigations of physiologists show that the muscles change in their constitution during exercise and that the internal thickness of the muscle may be relieved by rubbing the legs, by the application of heat or by repeated starting before the final start is made.

A CANCER FUND FOR CANADA

To commemorate the twenty-fifth anniversary of the accession of King George V to the throne, the governor general of Canada is inaugurating the raising of "the King George the Fifth Silver Jubilee Cancer Fund for Canada." When completed, the fund will be administered by a board of trustees set up for the purpose. The Canadian Medical Association has authorized the establishment of a department of cancer control, and it is hoped that the fund will provide the necessary financial aid to enable it to carry out its program. A study committee has been developed within the Canadian Medical Association under the leadership of Dr. Alexander Primrose to work out the plan of attack. The plans include the securing of funds, the propagation of knowledge concerning cancer and the methods of attacking it, the establishment of a library of cancer, and the making of grants to aid cancer study and research. In outlining the plan of attack, the following points are given special consideration: (*a*) The attack against the cancer cell and the chemical reactions that occur within it. (*b*) Cancer-producing substances —petroleum in various forms, the hormone estrin, and so on. (*c*) Facts regarding anticancer serum. (*d*) Hereditary factors in cancer. (*e*) Chemical substances that destroy the cancer cell without being harmful to the normal cell; e. g., lead salts. (*f*) Cobra venom. (*g*) Biochemical investigation, in particular the metabolism of carbohydrates as sources of energy. The bio-

chemical results of radiation on the living cells. (*h*) Immunity. (*i*) Grading of malignant tumors. (*j*) The cancer-producing properties of commercial lubricating oils. (*k*) The serum test for cancer. (*l*) Radium: proper dose and legitimate field for employment. The bomb. X-rays. This type of intensive effort should lead to considerable advancement in cancer control in Canada. It is believed that both the public and the medical profession will aid in the development of funds and in the promulgation of the work. The place of cancer on the list of causes of death emphasizes the necessity for more intensive activity than has thus far been developed in relationship to its control.

Medical Economics

COLLECTION AGENCIES

At various times in THE JOURNAL, physicians have been warned repeatedly to use extreme care in the selection of collection agencies and methods. It has frequently happened that the physician is duped by suave salesmen, whose promises cannot be substantiated, into signing an apparently innocent paper, which later is found to be a contract. Many of these contracts are in the nature of assignments which relieve the physician of all control and ownership of the accounts.

During a recent broadcast, a representative of the Better Business Bureau of Chicago presented some of the Better Business Bureaus' ideas and experiences with collection agencies and methods. The principal parts of this broadcast talk are given below:

"It has been said on good authority that a creditor is his own best collector, and, in the case of debts owing to doctors, dentists and other professional men, this is undoubtedly true. However, whether you are a professional man or a merchant, it would be indeed unusual if you could personally find time to collect all your outstanding debts. The task would be almost impossible.

"The alternate followed by most business men today is to turn over to a professional collection agency the job of collecting his past due accounts. Ordinarily, this service is rendered for a fee, sometimes a flat rate, but usually on a commission or contingency basis.

"About three years ago, Chicago was overrun by a small group of crooked collection agencies, which took many thousands of dollars from the community before their activities were terminated by the State's Attorney's office. They were openly operating against the law but were enabled to collect these large sums of money through a clever trick, which might be characterized as 'collecting from the creditor.'

"The procedure was usually about as follows: You would be approached by a salesman of one of these companies, who would tell you in glowing exaggerations what unusual success his company had experienced in collecting money. You need not pay the company anything until the collections had been remitted to you and there was no necessity for you to sign any contract or other written agreement. No doubt this type of presentation would appeal to almost any business man, most of whom had large numbers of outstanding accounts three years ago.

"You can see no objections to turning over to this man some of your accounts as a trial—and, of course, you picked out your oldest accounts and usually the ones which you had long since given up hope of ever collecting. Perhaps you smiled inwardly as you gave these accounts to the salesman, but the salesman was also smiling inwardly because he received a liberal commission for obtaining every one of your accounts. These salesmen's commissions were, in fact, so liberal that the offices of these gyp concerns were besieged every morning by men and women anxious to work for these companies. Little did they know of the reputation and methods of doing business of these fly-by-nights—all they knew was that their friends were making substantial commissions and why shouldn't they?

"On the day following the visit of the salesman, you receive a neatly typewritten letter from the company, acknowledging receipt of your accounts and assuring you that they would receive prompt attention. The 'prompt attention' was usually forthcoming about three weeks or a month later in the form of a telephone call from the company's office. It went something like this: 'Mr. Jones, we have just located a substantial bank account in the name of one of your debtors, and we would like to "tie it up" immediately to prevent his withdrawing any funds until your debt is paid. If you will advance $17.50 for legal expense, we will proceed immediately to collect your debt of $450. I will send our messenger to your office within the next few minutes to pick up your check, as no time should be lost.'

"While somewhat bewildered, you are so astonished to learn that this particular party from whom you had been trying to collect your debt for the past several years was clever enough to conceal a bank account outside the city that you give little thought to the possibility of the entire matter being a trick to obtain your money. Neither is there much opportunity given you to reflect, because the company's messenger is in your office within a few minutes after you have hung up the receiver. You reason that if you can collect $450 by spending $17.50, that certainly is good business, so the messenger receives your check. This same procedure may be repeated once or twice more before you come to the conclusion that the company is not acting in good faith. Usually, however, the average business man will hesitate before giving the company another check until he sees the results from the first one.

"Nothing further is heard from the company and your telephone calls are greeted by the various evasions popularly known as 'buck-passing.' 'Mr. So-and-So is out of the office and will call you back' or 'he is no longer with the company because we found he was crooked.' Personal calls at the office of the company result in nothing because you can never find any one in authority—he is always 'out.'

"When the State's Attorney's officers raided one of these fly-by-night concerns, the records of the company showed more than $1,000 a day was being collected by this means. The only substantial expense of the company was commissions paid to solicitors, for no trace of any actual collection efforts in the form of letters, garnishments, wage assignments or other legal procedure was found when the company's records were examined. The only money collected was taken from the creditors—not the debtors.

"Needless to say, there are no such companies operating in Chicago at the present time. However, there are a large number of collection agencies which are today operating on what is known as a 'shoe string.' These companies are operated by individuals who might make some effort to collect your debts. When they are successful, they usually retain most of what they collect for various 'fees,' 'legal charges,' and the like. It is a rare occasion when you can obtain a statement from the agency showing the status of your accounts, and if such a statement is ever forthcoming it will probably set forth collection charges far in excess of actual collections, so that you owe the company money.

"Examination of your written agreement will disclose a confusing mass of 'ifs, and buts.' Of course, you never read the agreement before you signed it, so that you have nobody to blame but yourself. If you take the trouble to dissect the various conditions in your contract, you will undoubtedly discover that the company has protected itself in every possible legal way and the various charges levied are all within the company's rights. Obviously, such collection service is of no value to you. The high pressure methods used by such companies in collecting your debts will invariably destroy your customers' good will and render them valueless as a future source of business. At the same time, you gain absolutely nothing and your debts must eventually be written off your books as a dead loss, even though the collection agency has collected in full.

"If you must employ the services of a collector, be certain that he is reliable. Regardless of whether he is a lawyer or a member of some association of collection agencies, investigate his past record and ascertain whether he has any satisfied clients—not clients who have just recently employed his services, but those who have been dealing with him for several years. Any reliable collection agency will gladly furnish you with such references."

Association News

THE ATLANTIC CITY SESSION

Section Hotel Headquarters

The Section on Obstetrics, Gynecology and Abdominal Surgery has designated the Hotel Dennis as its headquarters during the Atlantic City session of the American Medical Association, June 10 to 14. Members of the Section on Obstetrics, Gynecology and Abdominal Surgery are invited to make their reservations at the Hotel Dennis for the session.

MEDICAL BROADCASTS

Columbia Broadcasting System

The American Medical Association broadcasts on a western network of the Columbia Broadcasting System each Thursday afternoon on the Educational Forum from 4:30 to 4:45, central standard time. The next three broadcasts will be as follows:

March 28. This Is No April Fool, W. W. Bauer, M.D.
April 4. Negro Health Week, W. W. Bauer, M.D.
April 11. Sickness Insurance, R. G. Leland, M.D.

National Broadcasting Company

The American Medical Association broadcasts under the title "Your Health" on a Blue network of the National Broadcasting Company each Tuesday afternoon from 4 to 4:15, central standard time. The next three broadcasts will be as follows:

March 26. Tonics and Sedatives, Morris Fishbein, M.D.
April 2. Sickness Insurance, R. G. Leland, M.D.
April 9. Crying for the Moon, W. W. Bauer, M.D.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ALABAMA

State Medical Meeting at Mobile.—The sixty-eighth annual session of the Medical Association of the State of Alabama will be held in Mobile, April 16-18, with headquarters at the Battle House, under the presidency of Dr. William M. Cunningham, Jasper. The Mobile County Medical Society will be host to the society, and the following guest speakers will be included on the program:

Dr. Arthur Neal Owens, New Orleans, Skin Grafting: Its Relation to General Surgery.
Dr. Edward Nicholas DeWitt, Bridgeport, Conn., The Detached Retina.
Dr. Edgar Burns, New Orleans, Renal Calculi.
Dr. William B. McGee, New Orleans, Treatment of Severe Preeclampsia and Eclampsia with Ephedrine.

Dr. George Henry Semken, New York, will deliver the Jerome Cochran Lecture, Wednesday morning; his subject will be "A Consideration of Tumors of the Breast." On the same day, Dr. James S. McLester, Birmingham, President-Elect, American Medical Association, will speak on "Trends of Medical Practice." At a public meeting, Wednesday evening, Dr. Austin A. Hayden, Secretary of the Board of Trustees, American Medical Association, Chicago, will show a motion picture demonstrating the activities of the Association. Other physicians on the program include the following:

Theron K. McFatter, Dothan, Safety of Low Cesarean Section in the Obstetric Emergency.
Eugene Thames, Mobile, Chronic Undulant Fever.
Colvin C. Perdue, Mobile, Foreign Bodies in the Food and Air Passages.
William Hill McCaslan, Union Springs, The Nervous Child.
Thompson F. Wickliffe, Jasper, Deep Surgical Infections of the Neck.
Gordon C. Ussery, Roanoke, Status of Hysterectomy in Rural Surgical Practice.
Dan C. Donald, Birmingham, Acute (Hemorrhagic) Pancreatitis.
William W. Harper, Selma, The Enlarged Thyroid.
Claudius O. Lawrence, Clanton, Value of Local Applications in Diseases of the Respiratory Tract.
Amos C. Gipson, Gadsden, Treatment of So-Called Colitis in Infants and Children.
H. Earle Conwell, Fairfield, Problems Frequently Encountered in Recent Fractures.
Marion T. Davidson, Birmingham, Some Little Known Manifestations of Allergy.
Crawford H. Cleveland, Anniston, Chronic Hoarseness.
Gilbert F. Douglas, Birmingham, Ovulation, Menstruation, and Finding the "Safe Periods."
Cabot Lull, Birmingham, The Doctor and Life Insurance.
John L. Branch, Montgomery, Infections of the Hand.

The tenth annual meeting of the woman's auxiliary will be held at the Battle House, April 16-17. There will also be a symposium on pulmonary tuberculosis by Drs. Reuben Alec Brown, Montgomery, and James Otis Lisenby, Atmore.

ARIZONA

Bill Passed.—H. 88 has passed the house, proposing to create a board of naturopathic examiners and to regulate the practice of naturopathy. Naturopathy, which, the bill states, "includes all forms of physiotherapy, is hereby defined to be: A system of treating the abnormalities of the human mind and body by the use of drugless and nonsurgical methods, and includes the use of physical, electrical, hygienic, and sanitary measures incident thereto."

Bills Enacted.—The following bills have become laws: S. 15, repealing the laws regulating the distribution and possession of narcotic drugs and enacting what apparently is the uniform narcotic drug act; and H. 19, enacting a new pharmacy practice act which seems to prohibit physicians from dispensing drugs and medicines but permits them to administer personally "drugs and medicines carried or kept for emergencies . . . in order to supply the immediate needs of their own patients."

ARKANSAS

Bill Passed.—H. 218 has passed the house and senate, proposing to amend the medical practice act so as to authorize the boards of medical examiners, in their discretion, to license without examination diplomates of the National Board of Medical Examiners.

CALIFORNIA

Health Insurance.—The house of delegates of the California Medical Association, at a special meeting in Los Angeles, March 3, voted its approval of health insurance. A committee was appointed to cooperate with a committee of the state senate now studying the problem in framing legislation to establish a health insurance system, mandatory as to certain population groups and voluntary as to certain groups. The resolution set forth the following principles to be followed in the framing of the measure: (1) The patient shall have absolutely free choice of physician and hospital; (2) the medical profession shall determine the scope, extent, standards, quality, compensation paid for and all other matters and things related to the medical and medical auxiliary services rendered under the system; (3) there shall be no provision for cash benefits, and (4) the patient shall receive adequate treatment and his physician shall receive adequate compensation.

COLORADO

Bill Introduced.—S. 277 proposes to make it unlawful for any person to receive hospital care with intent to defraud the hospital of the amount due it for such care. It is to be prima facie evidence of intent to defraud for a patient to leave a hospital without paying his bill.

DISTRICT OF COLUMBIA

Memorial Service for Dr. Theobald Smith.—A memorial service was held at George Washington University School of Medicine, February 19, in honor of the late Dr. Theobald Smith, Princeton, N. J., director emeritus of the Department of Plant and Animal Pathology, Rockefeller Institute for Medical Research. Dr. Earl B. McKinley, dean of the medical school, reviewed the life and work of Dr. Smith. Following this service, the third lecture in the Smith-Reed-Russell series was presented by Dr. Thomas R. Boggs, associate professor of medicine, Johns Hopkins University School of Medicine, Baltimore. His subject was "Mycotic Infection of the Lung."

Medical Bills in Congress.—H. R. 6685, introduced by Representative Quinn, Pennsylvania, proposes to provide for the examination and registration of those who desire to engage in the occupation of beauty culture, which is defined to include, among other things, "the removal of superfluous hair, and the massaging, cleansing, stimulating, manipulating, exercising, or similar work upon the scalp, face, arms, or hands, or the upper part of the body, by the use of mechanical or electrical apparatus or appliances or cosmetics, preparations, tonics, antisep-

tics, creams, or lotions. . . ." H. R. 6735, introduced by Representative Norton, New Jersey, proposes to provide for the prevention of blindness in infants born in the District of Columbia.

GEORGIA

Bill Enacted.—S. 60 has become a law, repealing the laws regulating the possession, sale or distribution of narcotic drugs and enacting what apparently is the uniform narcotic drug act.

Fischer Prizes Awarded.—Drs. W. Frank Wells and Stacy C. Howell, Atlanta, were awarded the L. C. Fischer Prizes of the Fulton County Medical Society for 1934 at its annual banquet, January 3. Dr. Wells received the prize for the most original paper; his subject was "Modern Surgical Advances." Dr. Howell's paper on "Epinephrine—A Drug for Treatment of Glaucoma" was considered the best written. The prizes are awarded annually.

IDAHO

Personal.—Dr. Vonando G. Logan, American Falls, has been appointed health officer for Power County.——Dr. Harwood L. Stowe, Kimberly, has been appointed coroner of Twin Falls County to succeed the late Dr. Frank A. Dwight, Filer.

ILLINOIS

Bill Introduced.—S. 238, to amend the medical practice act, proposes to create a board of chiropractic examiners.

Heart Disease Leads in Mortality.—Heart disease accounted for 21,034 deaths in the total of 87,195 in Illinois for 1934, according to the state health department. A general mortality rate of 11.1 per thousand was noted for the year, a figure slightly higher than the average since 1929 but substantially lower than that for any previous year on record. The report stated that although the birth rate, 14 per thousand of population, was slightly higher last year than in 1933, the rise in mortality offset the gain, leaving an excess of only 23,000 births over deaths, the lowest on record. The maternal mortality rate (4.8 per thousand births) was the lowest on record, but the infant death rate of 53.2 per thousand births was noticeably higher than for 1933. A new low level was reached for mortality from tuberculosis, 4,102 deaths giving a rate of 52 per hundred thousand of population. There were sharp advances in mortality from infantile diarrhea and pneumonia. Second to heart disease was cancer, accounting for 9,638 deaths; nephritis, 8,156; accidents, 6,919; cerebral hemorrhage, 5,600; pneumonia, 5,901, and tuberculosis, 4,102. These seven causes accounted for substantially more than half of all mortality last year, and all but tuberculosis and cerebral hemorrhage were responsible for marked increases.

Chicago

Dr. Cort to Give Gehrmann Lectures.—William W. Cort, Ph.D., professor of helminthology, Johns Hopkins University School of Hygiene and Public Health, Baltimore, will deliver the Gehrmann Lectures of the University of Illinois College of Medicine, April 8-10. The titles of the three lectures are:

Studies on Ascariasis in Children in the United States.
Epidemiology and Control of Schistosomiasis (Bilharziasis) in Egypt.
Present Status of the Hookworm Problem in the United States.

Society News.—Dr. George W. Crile, Cleveland, discussed shock before the Englewood Branch of the Chicago Medical Society, March 5.——Speakers at the meeting of the North Side Branch of the Chicago Medical Society, March 7, were Drs. Andrew C. Ivy and Anton J. Carlson on "Anterior Lobe of the Hypophysis—Function and Clinical Pathology" and "Physiology of the Ovaries" respectively.——Speakers before the Chicago Pathological Society, March 11, included Drs. Frank M. Cochems and Theophil P. Grauer on "Squamous Cell Carcinoma, Leukoplakia and Concretions in a Megalo-Ureter."——Dr. Henry Kennon Dunham, Cincinnati, among others, addressed a joint meeting of the Chicago Roentgenological Society, Chicago Tuberculosis Society and the Chicago Tuberculosis Institute, March 14, on emphysema.——The Chicago Gynecological Society was addressed, March 14, by Drs. Edward H. Richardson, Baltimore, on "Abdominal Hysterectomy" and Noble Sproat Heaney on "Vaginal Hysterectomy."——The Chicago Ophthalmological Society was addressed, March 18, among others, by Dr. Leo L. Mayer and H. W. Magoun, Ph.D., on "Effects on the Pupillary Reaction of Lesions in the Posterior Commissure."——Dr. Samuel L. Gabby, Elgin, discussed "Dermatitis Probably Due to Dyes" before the Chicago Society of Allergy," March 18, and a review of recent literature on urticaria was presented by Drs. Francis L. Foran, Tell Nelson, Samuel J. Taub, Leon Unger, William L. Beecher and Samuel M. Feinberg.

INDIANA

Bill Enacted.—H. 490 has become a law, providing that on the commitment of a person to an institution for the insane he or she be rendered sterile.

Course in Otolaryngology.—The tenth annual two weeks course in otolaryngology of the Indiana University School of Medicine, Indianapolis, will be conducted April 15-27. The course will consist of complete and minute dissection of the head and neck with practical applications by Dr. John F. Barnhill, and twelve mornings of clinical instruction and surgery by Dr. Barnhill and members of the staff in otolaryngology of the medical school. Further information may be obtained from Dr. Willis D. Gatch, dean of the medical school.

Society News.—Dr. Walter A. Foreman, Rockville, addressed the Owen County Medical Society in Spencer, February 21, on "Early Diagnosis of Tuberculosis."——At a meeting of the LaPorte County Medical Society in Michigan City, February 21, Dr. Charles Marshall Davison, Chicago, discussed "Recurrent Cholecystitis Following Cholecystectomy."——Dr. Virgil H. Moon, Philadelphia, discussed "The Shock Syndrome in Medicine and Surgery" before the Indianapolis Medical Society, March 19. A symposium on diseases of the thyroid gland will be given, March 26; speakers will be Drs. Harold F. Dunlap, Cleon A. Nafe and Harold C. Thornton. A speakers' bureau is being organized for the society, its activities to be confined to Marion County.

Correction—Reciprocity with New York.—THE JOURNAL reported the establishment of reciprocity relations of Indiana with New York, March 16, page 929. Inadvertently, this item was taken from a column in the *Journal of the Indiana State Medical Association* containing news of twenty-five years ago.

IOWA

Bills Introduced.—S. 168, to amend the osteopathic practice act, proposes (1) to eliminate the provision of the present law which specifically denies osteopathic physicians and osteopathic physicians and surgeons the right to prescribe or give internal curative medicines, (2) to permit osteopathic physicians to practice obstetrics and minor surgery, and (3) to define osteopathic practice as "that method of rehabilitating, restoring and maintaining body functions by and through manual stimulation or inhibition of nerve mechanism controlling such body functions, or by the correction of anatomical maladjustment, and/or by other therapeutic agents, methods and modalities used supplementary thereto; but such supplementary agents, methods or modalities shall be used only preliminary to, preparatory to and/or in conjunction with such manual treatment," and to declare that such osteopathic practice is not the practice of medicine within the meaning of the medical practice act. S. 177 proposes to include marihuana within the scope of the laws relating to the sale, distribution or possession of narcotic drugs.

KANSAS

New County Health Officers.—The state department of health announces the following new appointments of county health officers:

Dr. Francis D. Kennedy, Norton, Norton County.
Dr. James H. A. Peck, St. Francis, Cheyenne County.
Dr. Frederick E. Dargatz, Kinsley, Edwards County.
Dr. William F. Schroeder, Newton, Harvey County.
Dr. Ernest J. Beckner, Goodland, Sherman County.
Dr. Charles E. Gaston, Frankfort, Marshall County.

Personal.—Dr. Marjorie G. Eberhart has resigned her position on the student health department staff at Kansas State Agricultural College, Manhattan, to become head of the physical education department at Central Normal College, Danville, Ind. She has been succeeded by Dr. Osee May Dill.——Dr. Joseph R. Betthauser, Hays, was elected president, recently, of the newly organized Ellis Doctors' Club, which is composed of the thirteen physicians in Ellis County. Dr. Harry R. Bryan, Hays, is secretary. The club, which holds monthly meetings, was created to cooperate with the county commissioners in the care of indigent sick.

LOUISIANA

Bill Enacted.—H. 16-XXXX has been enacted as Act No. 16, Acts, 1934, amending the penalty section of the uniform narcotic drug act, enacted recently by the second special session of the legislature, by making a violation of the act punishable by imprisonment at hard labor for not less than twenty months nor more than five years.

Society News.—Dr. W. Russell MacAusland, Boston, addressed the Orleans Parish Medical Society, January 21, on

"Mobilization of Ankylosed Joints by Arthroplasty." Speakers before the society, March 11, were Drs. James D. Rives and Laurence H. Strug on "Treatment of Hirschsprung's Disease by Spinal Anesthesia"; Emmerich von Haam and Louis Lichtenstein, "Incidence and Clinical Manifestations of Lymphogranuloma Inguinale in New Orleans," and Isidore Cohn, "Diagnosis and Treatment of Some Vascular Disturbances of the Extremities."

MARYLAND

Advisory Board for Department of Welfare. — An advisory committee was recently appointed for the newly created municipal department of welfare of Baltimore. Dr. Winford H. Smith, medical director, Johns Hopkins Hospital, was named chairman of the committee, and Dr. George Walker, vice chairman. Other members include Drs. Esther L. Richards and Harry S. McCard.

Additional DeLamar Funds.—The Johns Hopkins University School of Medicine, Baltimore, has received an additional gift of $150,000 from the estate of Joseph Raphael DeLamar, who died in 1918. A fund of $4,706,450, which has been paid to the medical school over a period of years under Mr. DeLamar's will, supports many activities, including the DeLamar Lectures in Hygiene at the Johns Hopkins University School of Hygiene and Public Health. The will provided that, after other bequests had been made, the residue was to be divided so that one third went to the medical school and another third to Columbia University College of Physicians and Surgeons. This is the authorization for the recent gift. The DeLamar Lectures were established "to give to the people of the United States generally the benefits of increased knowledge concerning the prevention of sickness and disease and also concerning the conservation of health by proper food and diet."

MASSACHUSETTS

Dr. Lord Becomes Professor Emeritus.—Dr. Frederick T. Lord, since 1930 clinical professor of medicine, Harvard University Medical School, was retired from the faculty as professor emeritus, January 1. Dr. Lord, who is 60 years of age, graduated from Harvard in 1897 and received his degree in medicine in 1900. He has been associated with the institution in a teaching capacity since 1905, when he was named assistant in clinical medicine. He was a member of the American Red Cross Commission to Serbia in 1917. He is president of the Massachusetts Tuberculosis League and a former president of the American Association for Thoracic Surgery.

Bills Introduced.—H. 1157 proposes to create a board of chiropractic examiners and to regulate the practice of chiropractic defined by the bill as "the science of spinal examination, the adjusting of the segments and articulations of the human spinal column by hand only." Chiropractors are to be prohibited from practicing obstetrics, from prescribing or administering drugs or medicines, and from performing surgical operations with the use of instruments. H. 1894 proposes that a commission composed of two senators, five representatives and four citizens be established to investigate and study the subject of health insurance and to report its findings to the general court.

MICHIGAN

Graduate Conferences. — The Wayne County Medical Society, Detroit Tuberculosis Sanatorium and Detroit Department of Health are sponsoring a series of graduate conferences in acute communicable diseases and tuberculosis at the Herman Kiefer Hospital, which began March 5. The conferences are presented by Dr. Bert U. Estabrook and associates in acute communicable disease and Dr. Bruce H. Douglas and associates in tuberculosis.

Personal.—Dr. Hubert M. Heitsch has resigned as director of public health of the city of Pontiac to accept a position on the medical staff of the new combined Chevrolet and Fisher Body plant at Baltimore, newspapers report.——Dr. Perry V. Wagley has been named acting medical superintendent of Pontiac State Hospital, succeeding the late Dr. Edmund A. Christian, who retired the day before his death.——Dr. Frederick McD. Harkin has been appointed health officer of Marquette to succeed Dr. Thurman R. Laughbaum, resigned. Dr. Harkin held the position in 1893.——Dr. Howard P. Blake, Bergland, has been appointed full time physician at the Marquette branch prison. He succeeds Dr. Foster A. Fennig, resigned, who held the position on a part time basis.——Dr. Frank P. Bohn, Newberry, was honored at a celebration, March 1, commemorating his completion of forty-five years in the practice of medicine.

MINNESOTA

Bill Introduced.—H. 1075, to amend the workmen's compensation act, proposes to add to the list of compensable occupational diseases "poisoning by carbon monoxide fumes or its sequelae."

Personal. — Mr. James H. Baker has been employed as executive secretary of the Hennepin County Medical Society, Minneapolis. Mr. Baker was formerly engaged in newspaper work.——Dr. Carl Gustaf Arvidson, Minneapolis, has been knighted by King Gustav of Sweden. Later he will receive the Order of Vasa.——Dr. Chauncey A. McKinlay, Minneapolis, has been named assistant editor of *Minnesota Medicine*.

Extension Course in Refraction. — The University of Minnesota School of Medicine will offer an extension course in refraction, April 1-28, designed especially for rural medical practitioners who wish to supplement their general practice by work in refraction and physiologic optics. The work will be under the supervision of the department of ophthalmology and has been arranged to furnish the elements of ophthalmology, the elementary physiology of vision, physiologic optics and testing and recording of vision. The mechanical problems of neutralization of lenses and different methods of determining refractive errors and muscle imbalance will be taken up. The theory of and practice in skiascopy and postcycloplegic refraction are also included.

MISSOURI

Bill Enacted.—S. 28 has become a law, prohibiting the cultivation, curing, preparation, distribution or possession of marijuana. It is not to be unlawful, however, for any licensed pharmacist to possess and to dispense the drug on the written prescription of a physician, osteopath, dentist or veterinarian.

Bills Introduced.—S. 148 proposes to authorize the sterilization of insane, idiot, imbecile, feebleminded or epileptic inmates of state institutions. H. 300, to supplement the workmen's compensation act, proposes to make it a misdemeanor for any person having charge of any medical or hospital record of any injured workman to refuse to permit such record to be inspected or copied by the workmen's compensation commission, the employer, the workman or his dependents, or any other party to any proceedings for compensation under the act.

Clinical Meeting.—The spring meeting of the Kansas City Southwest Clinical Society was held at the Hotel President, Kansas City, March 11. Guest speakers included Drs. Frederic W. Bancroft, New York, on "Clinical Deductions in the Handling of Fractures Obtained from the Study of Bone Repair"; Alfred W. Adson, Rochester, Minn., "Surgical Consideration of Essential Hypertension" (round table luncheon); Irvin Abell, Louisville, Ky., "Diagnosis and Treatment of Diverticulosis and Diverticulitis," and Charles L. Scudder, Boston, "Treatment of Fractures of the Neck of the Femur."

Society News.—Dr. Oswald P. J. Falk discussed "Management of the Heart in Hypertensive Disease" before the St. Louis County Medical Society, March 13.——Speakers before the St. Louis Medical Society, March 12, were Drs. Leonard T. Furlow on "Chronic Subdural Hematoma"; Park J. White Jr., "Prevention of Respiratory Infections in Children," and Harry W. Lyman, "Relation of Upper Respiratory Infections to the General Condition of the Patient in Infancy and Childhood."——A joint meeting of the Jackson and Wyandotte County medical societies was addressed, among others, February 12, by Dr. Carroll M. Pounders, Oklahoma City, on pediatric therapy.

NEBRASKA

Bill Enacted.—H. 147 has become a law, repealing the laws regulating the sale, possession or distribution of narcotic drugs and enacting what apparently is the uniform narcotic drug act.

NEW JERSEY

Enforcing the Medical Practice Act.—The state board of medical examiners reports numerous prosecutions during the past few months. Among several irregular practitioners who pleaded guilty and paid the penalty were the following:

Jules F. Blondiau of the "Modern Medical Associates," Jersey City.
Olive L. Schreibweiss, Plainfield, a nurse.
Alfred W. Reid, unlicensed chiropractor.
Irvin W. Kirk, whose license was revoked in 1933.
Simon Noveck, owner of a drug store, but not a registered pharmacist.
William Carl Hirsch of the "Church of Inner Truth," Secaucus.
Anthony Zurawski of the "Modern Medical Associates" of Newark.
Jerry Giffune of the "Men's and Women's Medical Office," Newark.

Personal.—Dr. Henry H. Kessler, Newark, delivered the Hunterian Lecture before the Hunterian Society of England, in London, January 14, on "The Contribution of John Hunter

to Rehabilitation of the Crippled and Disabled."——Dr. Paul Keller has resigned as executive director of Newark Beth Israel Hospital, Newark, to engage in private practice.——Dr. Louis Klein, Detroit, has been appointed to assume direction of all medical activities of the firm of Hoffman-La Roche, Nutley. Dr. Klein has occupied a similar position with Parke, Davis & Co. in Detroit, where he was on the medical staff of Harper Hospital and was also consulting endocrinologist to the Wayne County Juvenile Court.——Dr. William M. Brien, Orange, has resigned as first assistant medical examiner of Essex County, to become health officer of Orange. His successor is Dr. George P. Olcott Jr., East Orange.——Dr. John F. Hagerty, Newark, was the guest of honor at a dinner at St. Michael's Hospital, January 30, marking his retirement as medical director after forty years' service with the institution.

NEW YORK

Internships at Letchworth Village.—One year residencies for the study of mental deficiency are offered by Letchworth Village, Thiells, one of the New York state schools for mentally deficient persons, beginning July 1. Requirements include graduation from a class A medical school and a year's general internship. Applications should be sent to Dr. Charles S. Little, superintendent, Letchworth Village, Thiells, N. Y.

Bills Passed.—The following bills have passed the assembly: A. 195, proposing to amend the provisions of the vital statistics law which requires that the personal particulars called for in a certificate of birth shall be authenticated by the signature of the informant, who may be any competent person acquainted with the facts, by providing that such personal particulars shall be obtained from a competent person acquainted with the facts, and A. 445, proposing to safeguard the distribution of "dangerous caustic or corrosive substances" as defined by the federal caustic poison act, by requiring their labeling as "poison." S. 344 has passed the senate, proposing to amend that provision of the vital statistics law which requires that the personal particulars called for in a certificate of birth shall be authenticated by the signature of an informant, who may be any competent person acquainted with the facts, by providing that such personal particulars shall be obtained from such a person.

Bills Introduced.—S. 1556, A. 1935 and A. 2197 propose to prohibit any state, county or city hospital or any hospital supported in whole or in part by public funds to employ nurses or other employees for more than eight hours in any one day. S. 1593, to amend the medical practice act, proposes to make it unlawful for any one other than a licensed physician to conduct, direct, supervise or control the work or reports of a clinical laboratory, which is defined as "a laboratory in which tests are made on individual persons, their secretions, excretions, blood and tissues to aid in the diagnosis, prognosis, or treatment of the individual's physical or mental state or states." The provisions of the bill, however, are not to apply to the qualitative or quantitative analysis of urine by a licensed and registered pharmacist, or to a clinical laboratory director duly licensed to conduct, direct or supervise a clinical laboratory within the city of New York, or to any person who has conducted, directed or supervised a clinical laboratory in the state for a period of at least six months prior to the date this bill may become enacted.

New York City

Personal.—Dr. Paul Mazzuri, assistant medical director of the New York Life Insurance Company, retired February 28, having reached the age of 70. Dr. Mazzuri has been on the insurance company's staff since 1903.

The Janeway Lectures.—Dr. Gleb V. Anrep, professor of physiology, Egyptian University, Cairo, Egypt, will deliver the Edward Gamaliel Janeway Lectures at Mount Sinai Hospital, March 25 and 26. His subjects will be "The Duodenopyloric Mechanism in Relation to the Sympathetic Nervous System" and "The Coronary Blood Flow in Relation to Pulse Pressure."

Symposium on Scientific Education.—The science forum of the New York Electrical Society will present a symposium entitled "Scientific Education—What Is Wrong With It?" at its regular meeting, March 27. Speakers will be Harry Woodburn Chase, LL.D., chancellor of New York University; William E. Wickenden, Sc.D., president, Case School of Applied Science, Cleveland; Colin G. Fink, Ph.D., head of the division of electrochemistry, Columbia University, and Dr. Alan Gregg, director for the medical sciences, Rockefeller Foundation.

NORTH CAROLINA

Bill Passed.—H. 293 has passed the house and senate, proposing to amend the workmen's compensation act by making some twenty-five occupational diseases compensable; included among them are anthrax, compressed air illness, chrome ulceration, silicosis, asbestosis, tenosynovitis, bursitis, miners' nystagmus, and poisoning from arsenic, brass, zinc, manganese, lead, mercury, phosphorus, carbon bisulphide, methanol, naphtha, halogenated hydrocarbons, benzol, nitro amido derivatives of benzol, radium, carbon monoxide, sulphuric, hydrochloric and hydrofluoric acid.

Personal.—Dr. Bennie B. Dalton, Rockingham, has recently been appointed health officer of Richmond County.——Dr. Wyman Plato Starling, Roseboro, has been appointed health officer of Sampson County, succeeding Dr. Stephen Glenn Wilson, Clinton, who resigned to engage in private practice at Angier.——Dr. John W. Williams, Monroe, La., has been appointed health officer of Asheville to succeed the late Dr. Dan E. Sevier.——Dr. Albert S. Root was recently elected president of the Raleigh Academy of Medicine.——Dr. James B. Bullitt, professor of pathology, University of North Carolina School of Medicine, Chapel Hill, was elected president of the local chapter of the American Association of University Professors, recently.——Dr. Addison G. Brenizer, Charlotte, was recently elected commander of the Charlotte Post of the American Legion.

NORTH DAKOTA

Bills Enacted.—The following bills have become laws: H. 8, amending the chiropody practice act by defining a chiropodist as "one who examines, diagnoses and treats abnormal nail conditions, excrescences occurring on the feet, including corns, warts, callosities, bunions and arch disorders, or one who treats medically, mechanically or by physiotherapy in a chiropodic manner the human foot; S. 75, granting hospitals, supported in whole or in part by private charities and treating persons injured through the negligence of others, liens on all rights of actions, claims, judgments, compromises or settlements accruing to the injured persons because of their injuries.

OHIO

The Rachford Lectures.—Dr. Roy G. Hoskins, director of the Memorial Foundation for Neuro-Endocrine Research, Boston, delivered the fifth annual series of Benjamin Knox Rachford Lectures at the University of Cincinnati College of Medicine, March 21 and 22. His subjects were "Endocrinology of Today" and "Endocrine Factors in Personality."

Graduate Program at Akron.—The Summit County Medical Society held the first of four "Post-Graduate Days" planned for this year, February 20, at the Akron City Hospital. Sessions occupied the afternoon and evening and were attended by 180 physicians from fifteen towns. Among the presentations were the following:

Treatment of Tuberculosis in the Home, Dr. Clarence L. Hyde.
Nontuberculous Pulmonary Infections, Dr. Joseph N. Weller.
Traumatic Conditions of the Bladder and Urethra, Dr. Charles E. Jelm.
Skull Fractures and Injuries to the Head, Dr. Walter A. Hoyt.
X-Ray Diagnosis of Gastric Ulcers, Dr. Arthur H. Stall.

Dr. Charles E. Updegraff was chairman of arrangements for this program. The next will be held at People's Hospital in April.

Dr. Tuckerman Honored.—The Cleveland Academy of Medicine at its meeting February 18 awarded the title of honorary secretary for life to Dr. Jacob Edward Tuckerman in recognition of thirty-three years of continuous service to the academy in various capacities. Dr. Howard Lester Taylor, president, presented to Dr. Tuckerman an illuminated parchment on which was inscribed the action of the society, and Dr. George E. Follansbee paid tribute to his long service. Dr. Tuckerman became a member of the academy in 1903 and was appointed an alternate delegate to the Ohio State Medical Association the same year. From that time he has constantly maintained an official position, ranging from committee membership to the presidency of the academy.

OKLAHOMA

Bill Enacted.—H. 126, proposing to create a board of chiropody examiners and to regulate the practice of chiropody has become a law.

Bill Passed.—H. 46 has passed the house and the senate, proposing to require every hospital or physician treating a patient suffering from an injury caused by the discharge of a gun to report the facts to the proper police authorities.

Medical Assembly in Muskogee.—The Muskogee Academy of Medicine sponsored a two-day medical assembly, Feb-

ruary 26-27, with the following guest speakers, among others: Drs. Ernest Sachs, St. Louis; William T. Pride, Memphis; John O. McReynolds, Dallas; Arthur G. Schoch, Dallas; Barton A. Rhinehart, Little Rock, Ark., and Sidney J. Wolfermann, Fort Smith, Ark. A public meeting was held in the evening of February 27, at which Dr. McReynolds and Dr. Leroy Long, Oklahoma City, president, Oklahoma State Medical Association, were the speakers on care of the eyes and medical care of the indigent, respectively. Dr. Long made an address at a dinner given by the academy for the guests, on "Medical Integrity."

OREGON

Bills Passed.—H. 440 has passed the house and senate, proposing to amend the law requiring a male applicant for a license to marry to present a physician's certificate showing freedom from venereal disease and from mental illness or defect, by requiring such certificate from both parties to a proposed marriage. H. 373 has passed the house and the senate, proposing to authorize the state board of health to make such rules and regulations as it deems necessary for the operation of laboratories in which human or animal body fluids, secretions or excretions are examined for the determination of the presence or absence of an infectious agent. Every person, corporation or municipal corporation maintaining such a laboratory is to be required to register annually with the state board of health.

PENNSYLVANIA

Bills Introduced.—S. 490 proposes to authorize the sterilization of certain socially inadequate inmates of state institutions. H. 1262 proposes to make the records of any hospital concerning the stay and treatment of patients therein admissible in evidence in court for all intents and purposes without further proof thereof than their authenticity.

Society News.—Dr. John A. Kolmer, Philadelphia, addressed the Cambria County Medical Society, March 14, on "Syphilis from the Standpoint of the General Practitioner."——Drs. James J. Jefferson and Joseph P. Replogle, Johnstown, addressed the Westmoreland County Medical Society, February 14, on "Infections of the Hand and Forearm" and "Causes of High Mortality in Appendicitis," respectively.——Dr. Leon G. Zerfas, Indianapolis, addressed the Harrisburg Academy of Medicine, March 19, on "The Anemias."

Philadelphia

Anders Lecture.—Dr. Milton J. Rosenau, Charles Wilder professor of preventive medicine and hygiene, Harvard University Medical School, Boston, gave a James M. Anders Lecture before the College of Physicians of Philadelphia, March 6. His subject was "Specific Treatment and Prevention of Pneumonia."

Personal.—Dr. Ella B. Custer, who has practiced medicine for more than fifty years, was designated the outstanding citizen of the twenty-first ward in 1934 with the presentation of a silver plaque by the Roxborough-Manayunk Lions Club, February 25. The honor was the first of its kind and is to be an annual event hereafter.

SOUTH DAKOTA

Bill Passed.—H. 213 has passed the house and senate, proposing to repeal the laws regulating the sale, distribution or possession of narcotic drugs and to enact what apparently is the uniform narcotic drug act.

New Plan for Relief Administration.—South Dakota physicians and the state relief committee have inaugurated a new plan of budgeting federal relief money to the separate counties according to the number of families on relief. As conditions change each month, the amount will fluctuate, the *Journal-Lancet* reports. Two physicians and one dentist have been appointed in each county to audit all bills and recommend to the county relief directors the amount due each physician, dentist, nurse and pharmacist each month. When the bills for medical service exceed the budget, the amount available will be distributed pro rata.

TEXAS

Bill Introduced.—H. 640 proposes to make it the duty of parents or legal guardians of a child between 6 and 18 years of age to have the child examined to determine whether or not he has a defect in either sight or hearing such as to prevent him from receiving the full benefit of school work.

Society News.—Speakers at the meeting of the Dallas County Medical Society, March 28, will be Drs. John L. Goforth, on "Cancer of the Uterus from the Pathologist's Viewpoint"; Charles Frank Brown, "Hypothyroidism in Pregnancy" and James G. Poe, "Convulsions During Operation Under General Anesthesia."

VERMONT

Bill Introduced.—H. 288 proposes to accord to physician hospitals and nurses treating persons injured through the fau[lt] of others liens on all rights of action, claims, judgments, compromises or settlements accruing to the injured persons by reason of their injuries.

Bills Passed.—H. 264 has passed the house, proposing to supplement the chiropractic practice act, by permitting the board of chiropractic examiners to revoke the licenses of licentiates or to refuse licenses to applicants who have been convicted of criminal abortion or who have been guilty of professional or dishonorable conduct, which the bill states is (1) advertising which has a tendency to deceive the public, (2) conviction of any offense involving moral turpitude, (3) habitual intemperance and (4) habitual use of habit-forming drugs. H. 162 has passed the house, proposing to limit to licensed physicians and registered pharmacists the retail sale or distribution of articles or medicinal preparations that may be used as prophylactics or contraceptives.

WASHINGTON

Bills Introduced.—H. 580 proposes to establish a state hospitalization board to provide for the construction, operation and maintenance of experimental hospitals, clinics and outstations in King County, in Clallam County, and in the eastern part of the state. Apparently, all types of medical and dental services are to be available without cost to the public in the hospitals, clinics and outstations just noted. Establishment of these experimental units is to be conditioned, however, on the receipt from the Federal Emergency Relief Administration of $500,000 and the expenses of the experimental units are to be financed entirely from this fund. The state hospitalization board is also to propose to the 1937 session of the legislature a complete plan for dividing the state into hospital districts and for establishing and maintaining an adequate public hospital system within each of the districts to be established. H. 583 proposes to create a social service department of the state of Washington to render free medical, hospital and dental services "of all kinds known to science in all cases of sickness, accident, and childbirth to all residents of the state." The department is to have the power to take over all hospitals, public and private, in the state. All physicians in the state are to treat under the direction of the department and are to be paid an annual salary in accordance with the number of years during which they have been licensed to practice medicine. Every person "earning a living" is to be obliged to make monthly contributions to the state of from $2.50 to $5, depending on the number of persons dependent on the individual. S. 331 proposes to regulate the practice of naturopathy and to create an independent naturopathic examining committee. Licentiates are apparently to be permitted to practice obstetrics, "traumatic" surgery and minor surgery, and to use anesthesia in obstetric and traumatic and minor surgical cases.

WISCONSIN

Bills Introduced.—A. 414 proposes that any person declared by the state board of health to be a typhoid carrier, who does not conduct himself in the manner required by the board, may be committed to any institution where proper care and maintenance can be provided and may be confined until the board consents to discharge. If a typhoid carrier is prevented from engaging in any gainful occupation, he may be awarded up to $30 a month to compensate him for loss of earning power. A. 421, to amend the laws relating to the practice of chiropractic, proposes to provide that the provisions of the basic science act shall not apply to applicants for licenses to practice chiropractic. The bill proposes that the chiropractic board, instead of the basic science board, examine such applicants in anatomy, physiology, pathology and diagnosis. A. 422 proposes to amend the laws relating to the practice of chiropractic so as to raise the annual registration fee required of chiropractors to $5 and to make the annual registration of a chiropractor contingent on his attending within the preceding year at least one of the two-day "educational" programs conducted by the Wisconsin Chiropractic Association. A. 451 proposes to create a board of naturopathic examiners and to regulate the practice of naturopathy. All present practitioners are to be issued a certificate of registration in the basic sciences without examination and are to be licensed by the naturopathic board also without examination.

GENERAL

Early Diagnosis Campaign.—The National Tuberculosis Association is sponsoring its annual early diagnosis campaign, beginning April 1. The campaign will be carried on this year with the slogan "Fight Tuberculosis with Modern Weapons," and will stress particularly the fact that "the treatment of tuberculosis in all cases must be based on diagnosis."

Admiral Grayson Named Chairman of Red Cross.—Admiral Cary T. Grayson, Washington, D. C., has been named chairman of the American Red Cross, succeeding the late John Barton Payne. Dr. Grayson is a graduate of the University of the South Medical Department, Sewanee, Tennessee, class of 1903. In that year he joined the U. S. Navy Medical Department, with which he was associated until his retirement in December 1928 with the rank of rear admiral. He was attending and consulting physician to the Naval Dispensary, Washington, during the Roosevelt and Taft administrations, and served as physician to President Woodrow Wilson. Admiral Grayson is 56 years of age.

Advisory Service on X-Ray Technic.—The National Tuberculosis Association announces that a study on the standardization of x-ray technic which it has conducted for the past ten years has now reached the point at which effective advisory service can be offered to the x-ray departments of hospitals and sanatoriums. The research has been done at the Moore School of Electrical Engineering at the University of Pennsylvania under the direction of Mr. Charles Weyl. The objectives are based on the following principles, according to the announcement:

1. That a standardized system of technic determined on scientific bases should be used for the making of all diagnostic films in order to obtain (*a*) films having characteristics conducive to maximum interpretability, and (*b*) films of the same patient which will be comparable when taken at different times and also when taken in different laboratories.
2. That diagnostic roentgenography should be accomplished with a maximum of economy in cost of apparatus, technical apparatus, technical manipulation and supplies, with especial emphasis on economy in the number of films.

Registry of Physical Therapy Technicians.—With the acceptance of applications of qualified technicians for examination, the American Registry of Physical Therapy Technicians, in process of organization for more than two years, has begun to function. Applications will be issued only on written request to the registrar, Marion G. Smith, B.S. Examinations will be held May 4 and July 13 in New York, Philadelphia, Chicago, St. Louis, New Orleans, Los Angeles and San Francisco, and on September 9 in Kansas City. The registry was promoted to register and certify those technicians who meet its requirements. It is directed by a board of registry, composed of seven members:

Dr. William Bierman, New York, chairman.
Dr. Harold M. F. Behneman, San Francisco.
Dr. John S. Coulter, Chicago, associate professor of physical therapy, Northwestern University Medical School, Chicago.
Dr. Frank H. Ewerhardt, St. Louis, assistant professor of physical therapy, Washington University School of Medicine, St. Louis.
Dr. John S. Hibben, Pasadena, Calif.
Dr. Frank H. Krusen, Philadelphia, associate in medicine, Temple University School of Medicine.
Dr. Nathan H. Polmer, New Orleans, assistant professor of clinical medicine, Tulane University Graduate School of Medicine.

In addition, there is an advisory board composed of representatives from national organizations interested in the work of physical therapy technicians and the physicians who use physical therapy in their specialties. This board is also composed of seven members. A regional board will comprise two or more members, according to the local requirements. There will be two classes of certification: physical therapy technicians and junior physical therapy technicians. A certificate may be revoked at the discretion of the board of registry, and all registered technicians and assistants will be required to comply with the code of ethics as defined by the American Congress of Physical Therapy.

Society News.—The annual meeting of the American Association on Mental Deficiency will be held at the Palmer House, Chicago, April 25-27. Physicians are invited to attend all sessions. Complete information on the program may be obtained from Dr. Groves B. Smith, secretary, Godfrey, Ill. ——Dr. Ralph C. P. Truitt, Baltimore, was elected president of the American Orthopsychiatric Association at the annual meeting in New York, February 22-23; Willard C. Olson, Ph.D., Ann Arbor, Mich., vice president, and Dr. George S. Stevenson, New York, secretary.——The twentieth annual convention of the Catholic Hospital Association of the United States and Canada will be held at Creighton University, Omaha, June 17-21.——The twenty-third annual meeting of the Eugenics Research Association will be held at the American Museum of Natural History, New York, June 1.——The annual meeting of the National Medical Association will be held in New Orleans, August 11-17.——The twenty-fourth annual National Safety Congress will be held in Louisville, Ky., October 14-18. ——The Eastern Section of the American Congress of Physical Therapy will meet in Baltimore, March 29-30. The program will open in joint session with the Baltimore City Medical Society and will be presented by the following physicians, among others: Drs. Frank H. Krusen, Philadelphia, "Light Therapy"; Henry H. Ritter, New York, "Physical Therapy in Traumatic Surgery"; William Bierman, New York, "Short Wave Therapy"; Thomas P. Sprunt, Baltimore, "Physical Therapy from the Standpoint of the Internist," and Allen F. Voshell, Baltimore, "Treatment of Delayed Union of Fractures."

Medical Bills in Congress—*Changes in Status:* H. R. 2827 has been reported to the House (Rept. No. 418). The bill proposes to direct the Secretary of Labor to provide for the immediate establishment of social insurance to provide compensation for all workers and farmers who are unable to work because of sickness, old age, maternity, industrial injury or other disability. H. R. 6718, the Agricultural Department appropriation bill, has been reported to the House (Rept. No. 385). This bill, among other things, authorizes an appropriation of $1,515,879 for the enforcement of the Pure Food and Drugs Act, an increase of $354,402 over the appropriation for the preceding fiscal year. S. 2024 has been reported to the Senate (Rept. No. 333). This bill would authorize the President to designate Colonel William L. Keller, Medical Corps, United States Army, on his retirement from the active list, as consultant in surgery at the United States Army Medical Center. *Bills Introduced:* S. 2214, introduced by Senator Thomas, Oklahoma, and H. R. 6625, introduced by Representative Rogers, Oklahoma, both bills being introduced by request, propose to confer jurisdiction on the United States District Courts over Osage Indian drug and liquor addicts. H. R. 6688, introduced by Representative Hennings, Missouri, proposes to prohibit the sale, possession and transportation of cannabis and its derivatives and compounds, except when sold, possessed or transported for medicinal and lawful uses by the producer or manufacturer thereof or dealer therein to licensed physicians, surgeons, dentists, pharmacists, druggists and veterinarians, under such rules and regulations as may be prescribed by the Commissioner of Narcotics. H. R. 6769, introduced by Representative Hoeppel, California, proposes to grant the benefits of veterans' legislation to maimed, blind or helpless retired personnel of the Army, Navy, Marine Corps and Coast Guard, in the furnishing of artificial appliances and allowance for attendants.

Government Services

Acting Director of Division of Maternal and Child Health

Dr. Ethel C. Dunham, associate clinical professor of pediatrics, Yale University School of Medicine, New Haven, has been named acting director of the division of maternal and child health, U. S. Children's Bureau. Dr. Dunham graduated from Johns Hopkins University School of Medicine, Baltimore, in 1918. For the past eight years she has devoted much of her time to research on the diseases of new-born infants.

Examination for Entrance to Public Health Service

The U. S. Public Health Service announces that an examination will be held, April 8, for entrance into the regular corps of the service as assistant surgeon. Applicants must be graduates of class A medical colleges and under 32 years of age. They must have completed a year's internship or have had two years of private practice by July 1. Sub-boards will be appointed for the examination so as to eliminate travel as far as possible, which if necessary must be made at the candidate's expense. Physicians who wish to take this examination should make a request to the surgeon general, U. S. Public Health Service, Washington, D. C., for the necessary forms and other information.

CORRECTION

Nobel Prize Winners in Medicine.—The name of Dr. William P. Murphy of Boston was inadvertently omitted in the Current Comment entitled "Nobel Prize Lectures on Anemia" in THE JOURNAL, March 9, page 838. The Nobel Prize for 1934 in medicine was awarded conjointly to Drs. Minot, Murphy and Whipple for their work on anemia.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 23, 1935.

A Salaried Service of Municipal Midwives

The Joint Council of Midwifery, which is representative of the important medical and nursing societies, has issued a report on the desirability of establishing a salaried service of midwives, under the local authority in all areas not already served by salaried midwives. The cost of the service, as far as practicable, is to be met by fees charged by the authority of local voluntary organization for the services of the midwife. The council holds that the nursing in every maternity case should be conducted by a qualified midwife and that unqualified persons should not be permitted to nurse in maternity cases for gain. It should be the duty of the local authority to provide that midwives are available as maternity nurses for any patient who has engaged a physician for her confinement but is unable to afford this additional expense. But it is not intended to interfere with the continuance in practice of independent midwives. Midwives entering this municipal service should receive adequate pay, allowances and pension rights and be accorded the same status in every respect as health visitors. The average number of cases that a midwife would be expected to attend should not exceed eighty a year. After this new act has come into operation the local authority should require that midwives in independent practice who, from age or physical or mental infirmity are unable to carry out satisfactorily midwifery practice, retire on receiving an adequate pension. Every midwife should be required to take a refresher course, including, if necessary, two months' residence in a training institution, at intervals not exceeding seven years.

THE INADEQUACY OF THE PRESENT REMUNERATION OF MIDWIVES

Owing to the large number of midwives in practice and the necessarily small fees paid by poor persons, the remuneration of midwives is entirely inadequate. The estimated number of salaried midwives now is 6,255 and of independent midwives 9,187. In 1929 a government committee, which reported on the training and employment of midwives, gave the average number of cases attended per midwife as slightly over forty and suggested that the average gross earnings varied from $450 to $600 a year. It is estimated that the position is much worse today, the average being estimated at $400 and in some cases as low as $250. Assuming that in future a midwife will attend every case, whether a physician is in charge or not, the number of municipal midwives likely to be required is estimated at 4,000. In addition, part time midwives or district nurses would probably have to be retained by means of a subsidy in semi-rural areas not covered by nursing associations.

Hugh Owen Thomas and an American Surgeon

In the months before his death in 1933, Sir Robert Jones discussed with his son-in-law, Mr. Frederick Watson, the publication of a centenary volume on the life and principles of Hugh Owen Thomas, his uncle and teacher. A personal study of Thomas by Mr. Watson has now been published, and a companion book on Thomas's surgical work by Mr. McCrae Aitken, an orthopedic surgeon and colleague of Sir Robert Jones, is in preparation. Though this biography has been so long delayed—Thomas died in 1891—no man deserved one more and no achievement in the whole range of surgery is more interesting. A frail little man, who for thirty years carried on an arduous general practice among the poor of Liverpool dockland without ever taking a holiday and without the advantage of a hospital appointment, revolutionized the treatment of tuberculous joints and laid a large part of the foundation of modern orthopedic surgery. The son of a Welsh bone setter and descended from a line of bone setters, he was regarded as one by the surgeons of his day and looked down on. It is interesting that an American surgeon, John Ridlon, was one of the first to appreciate Thomas's work. Mr. Watson quotes Dr. Ridlon's description of his first visit to Thomas in 1887. "I said 'Mr. Thomas, I have read your book on hip, ankle and knee and I have come over 3,000 miles to find out whether I am a fool or you a liar.' There was a twinkle behind the thick lenses and he said 'I think we'll find that out in half an hour.' Thus began two wonderful days. He let me follow him to every patient." Later Dr. Ridlon visited the clinics of all the well known orthopedic surgeons in Great Britain, and this is his verdict: "Not one of them had a kindly word to say of Thomas. But I was able to compare their work with his. One could gain more useful knowledge following Thomas around for an hour than elsewhere in Great Britain for months." In 1933 Dr. Ridlon wrote: "To my mind one of the greatest things Robert Jones ever did was to make the main principles of Hugh Owen Thomas acceptable to the profession." It is interesting in this connection that the importance of Jones's work was appreciated in other countries and particularly in America earlier than in England. The same was true of Lister. It was not until the war that Jones reached the pinnacle of his fame.

Financing Hospitals by Sweepstakes

In previous letters, details were given of the immense sums obtained for Irish hospitals by taking advantage of the gambling spirit of the world. The latest estimate, given by Sir John Gilmour the home secretary, in parliament shows that approximately $224,500,000 had been subscribed up to 1934 and that of this sum $38,000,000 has been allocated to hospitals. The greater part of the difference between these two sums is due to prizes (about two thirds of the total subscribed), expenses and a considerable sum in the form of revenue charged by the Free State government. The greater part of the money comes from other countries than Ireland and the major part of this from Great Britain. An attempt is now being made to stop this drain by making the sale of sweepstake tickets illegal in Great Britain, with what success cannot yet be said. Evasion of course is not difficult.

Steel Hats for Miners

During the great war, steel helmets were introduced to prevent the many serious casualties of bullet wounds of the head. It is curious that the value of this device for coal miners, of whom thousands are injured every year in this country by the falling of rocks, has not previously been recognized. During the last few days the unfamiliar figures of miners in black steel helmets has been seen in the streets of the Derbyshire and Notts colliery towns. Insurance companies and mine owners are now making arrangements for the general use of these helmets. They recognize that this will mean fewer compensation claims. Experiments have been made to produce the lightest and most efficient head protection, and a helmet has been produced which weighs only 12 ounces and will withstand a weight of 9 pounds dropped from a height of 8 feet. The helmets have a shield to protect the neck and are covered with a special composition. The steel lining is of great strength. The helmets cost 66 cents, of which the miners pay 18 and the insurance companies and the mine owners 24 cents each. Other protective devices being introduced are specially made gloves to prevent hand wounds and reinforced boots to prevent foot injuries.

PARIS

(From Our Regular Correspondent)

Feb. 15, 1935.

Transfusion of Refrigerated Citrated Blood

In Paris, the transfusion service is well organized. One of the many large public hospitals serves as a center, from which grouped and adequately tested donors are available at all times. This service will be described in a future letter. In smaller cities such as Bordeaux in the south of France, an effort has been made to utilize the blood of donors (universal group), which has been collected in flasks and kept liquid with the aid of a 10 per cent sodium citrate solution.

Jeanneny and Vieroz, at the Dec. 5, 1934, meeting of the National Surgical Society, reported the details of how such blood is kept in a refrigerator at 2 C. (35.6 F.). The blood can be utilized only during a period of twenty days after being placed in the refrigerator.

In only six of seventy cases were any reactions observed, in the form of a severe chill with slight fever (one case), slight chills without fever (four cases) and a feeling of paresthesia (one case). The simplicity of the technic of collecting the blood and its administration renders it available for city hospitals, where much time may be lost in making the various tests, especially those for syphilis.

Examination of the refrigerated blood reveals no changes in its components.

Prevention of Tuberculosis with B C G Vaccine

As a tribute to the memory of his associate Professor Calmette, Professor Guérin reported, at the January 15 meeting of the Academy of Medicine, some statistics on the employment of the B C G vaccine in France.

During the first ten months of 1933 there were 110,486 primary vaccinations and 13,909 revaccinations; during a similar period in 1934 the number of primary vaccinations had risen to 136,544 and of the revaccinations to 20,819. Vaccination of children over 2 years of age and of adults who do not react to tuberculin was begun towards the end of 1933. It consists in giving, by mouth, one ampule of the vaccine; 1,516 cases have been treated by this method. Boisseau and Nodenot in France and Scheel in Norway have shown that over 50 per cent of adults become allergic after being given the vaccine in this way. No ill effects have ever followed use of the B C G vaccine. The mortality from all causes of infants between the ages of 1 and 12 months is one half less in the case of those who have been than in those who have not been vaccinated. In families in which tuberculosis exists, the morbidity is eight times less in infants who have been than in the case of those who have not been vaccinated. The distribution of vaccine has been authorized in thirty-four countries exclusive of France. With the exception of a few countries in which vaccination is limited to children born of tuberculous parents or obliged to live among tuberculous individuals, all these countries extend the vaccination to all children, whether they live in surroundings where there is danger of contagion or not.

Failures in the use of the B C G vaccine as a preventive measure against tuberculosis are due to three causes:

1. There are a certain number of individuals who are refractory to any type of vaccination, such as that against typhoid or smallpox. An explanation of why persons in this group do not develop immunity is still lacking.

2. It is essential to remove new-born infants, who have been vaccinated, for a period of at least six weeks from contact with tuberculous individuals.

3. The majority of pathogenic organisms are destroyed and carried away by phagocytosis. This is not true for the tubercle bacillus and can be demonstrated experimentally. Calmette and Guérin have shown that in animals as well as in human beings the tubercle bacilli are excreted by the bile in both sexes and also by the mammary secretion in the female. In persons vaccinated with the B C G vaccine, and who then are subjected to virulent additional tuberculous infection, the bacilli are eliminated often without giving rise to macroscopic lesions. In the case, however, of severe and prolonged infections, if the number of bacilli that are absorbed is a larger amount than the organism can normally eliminate, there will be an "accumulation" of tubercle bacilli in the lymphatics and a possible production of genuine tuberculous lesions, which however are usually of a character that do not develop.

The part played by these three causes of resistance to vaccination has been demonstrated by animal experiments, especially those of the bovine type. It is probable that the same processes explain the resistance in the human being.

Complications of Pregnancy

Some interesting cases were reported at the Nov. 5, 1934, meeting of the Paris Obstetric and Gynecologic Society by Le Lorier and Levy-Solal.

Le Lorier reported a case of a woman, aged 40, in whom labor during her first pregnancy had been induced because of a severe influenzal bronchopneumonia. During a second pregnancy, severe pyelonephritis showed no improvement after the use of inlying ureteral catheters for fifteen days. The pregnancy was interrupted at the fifth month because of uremic symptoms and high blood urea. Spontaneous expulsion of the fetus occurred during the third pregnancy, complicated by recurrence of renal infection. Premature delivery during the fourth pregnancy was also accompanied by pyelonephritis of less intensity. Following this pregnancy, the blood urea gradually decreased during a period of three years from 279 mg. per hundred cubic centimeters to practically normal, 45 mg. During the fifth pregnancy the blood urea was only 38 mg. per hundred cubic centimeters. The patient was given a diet of vegetables, cereals, fruits and fermented milk. The pregnancy was without incident and she was delivered of a normal child at term. The case illustrates the gradual decrease in intensity of the renal infection in spite of evidence of an involvement, at an earlier period, of the renal parenchyma. The latter, although very marked during the fourth pregnancy, had also improved.

A similar case was reported by Levy-Solal, Sureau and Lauret. The patient was first seen during the sixth month of pregnancy, during an attack of severe renal infection with a blood urea of 170 mg. per hundred cubic centimeters. But little improvement followed the use of inlying ureteral catheters, although some retention had been found on both sides at the first ureteral catheterization. The blood urea rose as high as 250 mg. per hundred cubic centimeters. The estimation of chlorides in the blood (globular and plasma) revealed a ratio only slightly below normal. To restore the ratio to its normal figure, rechloridation was instituted in the form of salt solution given both subcutaneously and intravenously. The persistent emesis ceased and the diarrhea decreased markedly but the general condition was so alarming that evacuation of the uterus seemed indicated, but labor occurred and a living child weighing 1,700 Gm. was born. The blood urea, which was 250 mg. on the day of the confinement, decreased to 38 mg. on the tenth day. The use of inlying ureteral catheters was of no benefit in this patient. The high percentage of blood urea and its rapid recession seem to indicate that the renal parenchyma has not been seriously affected. The high blood urea was apparently only a temporary phenomenon, comparable to similar observations in postoperative cases. The rechloridation relieved the vomiting and diarrhea but had no influence on the high blood urea; but such treatment is to be recommended whenever inlying catheters do not give relief and the blood urea remains

high. Emptying the uterus is indicated when neither urologic methods nor rechloridation result in a drop in the high urea content of the blood.

A third instructive case, which raises the question as to the existence of supernumerary ovaries, was reported by Levy-Solal, Sureau and Lauret. The patient was a primipara, aged 21, who was in the first stage of labor on admission to the hospital, without engagement of the head. A mass the size of a large orange could be felt in the posterior culdesac, independent of the uterus. A diagnosis of ovarian cyst obstructing the head from entering the pelvis was made, and laparotomy was decided on. It revealed the presence of a dermoid of the right ovary, the size of an orange, with a short pedicle. A similar cyst of the left ovary, the size of a child's head at term, was present, a portion extending into the culdesac of Douglas. Not the least trace of ovarian tissue was visible, even on microscopic examination of the two dermoids. Either the dermoids must have developed during the pregnancy or there had been a supernumerary ovary. Various authors estimate that these are present in 4 per cent of women. These supernumerary ovaries are found attached to the ovary or they occur somewhere along the line of migration of the ovary in the embryo. They may be multiple and of variable size. Their presence explains the persistence of menstruation after bilateral ovariotomy.

On account of the patient's age, a cesarean section was performed after removal of the bilateral ovarian dermoids and an infant weighing 3,000 Gm. was delivered.

In the discussion, Faure reported a similar case in a woman, aged 28. Following removal of the dermoid cysts on both sides in the sixth week of pregnancy, the woman was delivered at term.

BERLIN

(From Our Regular Correspondent)

Jan. 28, 1935.

Reorganization of Student Activities in the Universities

A recent letter (THE JOURNAL, January 12, p. 132) gave an account of the struggles that have been going on in the student bodies of the universities. Since then, many changes have been made that will lead possibly to a greater stability. The struggle for supremacy, fought out between the German student body, as represented by certain student fraternities, and the national-socialist party, has been ended now by an executive order from the federal minister of public instruction (Rust). This decision releases the German student body from the duty of participating in the special training course designed to develop political insight and broader world views. This duty now need be fulfilled only by the members of the National-Socialist Student League. The purpose of this training is to create uniform political and world views to aid the students in forming their opinions. The general student body will not be compelled to enter a "kameradschaftshaus," as was originally planned. The fraternities have secured unquestionably greater liberty of action, although they are not permitted freely to air their political views. In keeping with this decision, the director of the National-Socialist Student League has declared that the semester must be devoted primarily to scientific study and that he is opposed to the suggestion that "in the form of weekly political lectures the students receive from one to one and a half hours of instruction in national socialism, as such a plan might lead to a degeneration of our intellectual life and to false conceptions of the true aims of a university." This denotes a wide departure from previous uses. During the vacations, however, the students will be brought together in camps, where they will receive such training as will make of them "true champions of national socialism." This director makes then some interesting confessions: "During the past year and a half, the student has been tossed about to such an extent that he has lost most of his faith in attempts to direct the thinking of students. A reawakening of this faith I regard as a necessity, since leadership without the confidence of one's followers is not true leadership but dictatorship."

The Deutsches Studentenwerk, a self-help organization for the aid of needy students, for whom the society procures opportunities to make a little extra money, has been reorganized by ministerial decree and placed under the control of the ministry. Its announced purpose now is "to provide every person possessing high intellectual gifts, irrespective of origin or financial status, an opportunity to attend a German university." The society receives now, in addition to voluntary contributions, certain sums from the students and from the government. It has, however, lost the right to administer its own affairs.

University Sports

With the beginning of the winter semester, the new university regulations pertaining to participation in sports went into effect in all the universities of the reich. Compulsory participation in gymnastic exercises and various sports, during the first three semesters, deserves special mention. Only in exceptional cases will students be excused from such participation (time spent in the arbeitsdienst, or work service, may be taken into account). The fundamental training for both sexes, during the first semester, consists of general body building, work in the gymnasium, cross country runs (sometimes in groups); in the second semester, of the so-called *fünfkampf-training,* and rifle practice, and, in the third semester, of group contests, swimming exercises and practice that will fit them for the rescuing of drowning persons. In the future, no student who has not met the requirements of the "fundamental training" will be permitted to continue with the studies of the fourth semester or become a candidate for any degree. After fulfilment of these conditions, a student will receive a badge. It is also planned to organize special sport events of the universities.

University Study Without Attendance at a "Gymnasium"

In a few special cases persons will be permitted to enter a university without having previously attended a "gymnasium." The minister of public instruction, in order to afford a few of the most talented sons of workmen an opportunity to attend a university, has consented, at the request of the German student organization, to allow twenty members of the "Hitler-Jugend" and of the Arbeitsdienst (work service) to be admitted to the student body without presenting a diploma of a "gymnasium." Under certain conditions they may be permitted, after two semesters, to matriculate as regular students. The intellectual training of these workmen's sons will be carried on with the cooperation of the student organization and the Deutsche Dozentenschaft, or association of faculty members. The funds for such university study will be furnished by the Deutsches Studentenwerk. For the training of these candidates the universities of Heidelberg and Königsberg are being considered.

University Entrance Requirements

According to an agreement between a Hitler-Jugend "führer" (leader) and the local school authorities, remission of the university entrance requirements, which for some time have been based on conditions quite apart from performance in school (THE JOURNAL, March 3, 1934, p. 710), is to be determined by considerations that concern the political usefulness, together with his type of character and his personal qualities. But the decision in such cases will not rest with the school but with

the führer of the Hitler-Jugend. Such an understanding would make it possible to help such führer to make up their deficiencies even though their performance might be only barely "satisfactory." This agreement is in line with a tendency manifest in the Hitler-Jugend to make university distinctions a political football, and it throws a floodlight on certain endeavors to bring German youth entirely under certain definite influences. The university authorities, however, in spite of their sympathy for the cause of the people, will hardly be willing to accept any such provisions.

Selective Diets in Hospitals

The experiences with a uniform diet for most patients in hospitals have not been universally satisfactory. In some institutions of Berlin an experiment has been made with an à la carte service, which permits the patients to choose the food they desire or which is prescribed. The results of this experiment are considered satisfactory; for example, in the Virchow Hospital, which has had a longer experience with the new system than some of the other institutions now using it. On an average, this hospital serves meals to 2,400 persons daily, including physicians and hospital personnel. Of this number, from 1,400 to 1,600 persons are served diets I or II, which permit the use of all foods, except possibly a few of the vegetables that are hard to digest. Diets III and IIIa presuppose a certain amount of selection. The old plan of serving uniform meals to all patients gave rise to many complaints. At first, the experiment was tried of serving the tuberculous patients, who are particular about their food, a selective diet, allowing them the choice of one of two articles. The complaints in this department ceased immediately. The experiment was then tried in other departments with equal success. Hence the new system was extended to all departments, and at the same time the number of meals at which a selective diet was permitted was extended to three a day. No complaints have developed since the introduction of the new system. There is no doubt that a diet satisfactory to the patients contributes to their recovery and influences their general well being. This selective system makes it possible to take some account of local peculiarities and special dishes, which are very marked in many parts of Germany. With the former uniform diet, menus calling for large amounts of meat were very expensive. After introduction of the selective diet there was no difficulty in offering a diet rich in meats, for it was found in a short time that the selective diet entails much less expense than the uniform diet, for which fact several reasons may be assigned. Principally, with the introduction of the selective diet, the expensive system of zulagen (certain side dishes) was abolished. Formerly the uniform diet was supplemented, if desired, by side dishes in the form of sweets, desserts, fruit, and the like, in order to give more variety to the meal. This system, however, added a great deal to the general expense. Now the patients have accepted the discontinuance of the side dishes as a system without complaint. Another source of economy is the fact that, under the new system, certain cheaper foods of high quality can be served more frequently than under the old system, since the patients do not need to select them unless they desire.

German-Spanish-American Medical Academy

In order to foster better relations between the German reich and the South American countries, the Deutsch-Ibero-Amerikanische Gesellschaft in Berlin is planning the creation of a medical academy. The idea is to establish in Berlin, with the cooperation of well known physicians and institutions of the reich, a special center that, it is hoped, will be of a nature to induce more physicians and patients from foreign countries to visit German cities and health resorts.

JAPAN

(From Our Regular Correspondent)

Jan. 26, 1935.

Outbreak of 1,000 Cases of Dysentery

In the city of Kawasaki, between Tokyo and Yokohama, with a population of 141,800, 1,258 dysentery cases occurred from January 2 to January 21. There first appeared all over the city children with symptoms of influenza accompanied by slight digestive trouble. After January 6, this disease began to attack the adults. On investigation, the disease was found to be dysentery. There were 147 deaths, and there are now more than 800 persons ill, but there is no sign of a further increase. The cause of the outbreak was at first thought to be the water, but no bacteria were found in it.

An Investigation of Encephalitis

At a meeting of the Japan Science Society, January 21, in Tokyo, Dr. Y. Iimura of the committee on encephalitis made a report after one year of research. Encephalitis breaks out here in August and decreases gradually toward September; two thirds of the outbreaks in the last ten years have taken place in August. The cases are found mostly in the western provinces. Many of the victims are professional workers, and the heads of families more often than other members. More cases are seen in the better class houses in high and dry places than in the low and damp places. When it is hottest, this disease occurs mostly in the villages; but when it is cooler, more are found in factory towns. After hard labor, mental or physical, especially in a burning sun, many have taken sick. It is still obscure whether the disease is infectious or not. Of the deaths during the last ten years, 64.8 per cent were among old women. The disease causes death in five days on the average when it is very hot. The density of population seems to have little to do with this disease. The heat of the previous month appears to have a great influence; for instance, when August is especially hot in some district, many cases have occurred there in September, a tendency present almost everywhere throughout the country. A relation between the disease and the rainfall has been noted. Less moisture and a longer period of sunshine cause a greater number of cases.

Professor Kubo Retires

It is widely regretted that Prof. Dr. Ino Kubo of the Kyushu Imperial University has reached the age limit and has to resign. For the first time in this university, a ceremonial clinical lecture was given by him, December 13, at the oto-rhinolaryngology lecture hall, which was founded by him in 1907. His last lecture was demanded by students of the lower classes who had never heard him lecture. The hall was overcrowded with students and graduates an hour before the lecture began. Those who couldn't get in filled two other halls, where they heard his lecture through loud speakers especially installed for the purpose. His subject was "The Essentials in Clinicians." He said: "To summarize my twenty-eight years of experience acquired in this room, I have examined during those years 133,539 outpatients and 16,941 inpatients. The spirit of my service to them will be described today. . . . The very first essential that we ought to have as clinicians is always to maintain a student-like attitude in diagnosing and treating patients. The second is that we should have the feeling of commiseration toward patients. Huefeland once said that the feeling of relieving a patient of his trouble is the principle of medicine. These I have had deeply implanted in my heart during these past years, trying ever to be faithful to them." He brought before the assembly eight persons who were cured of their trouble under his treatment recently. He explained each case, making a deep impression on every one present.

BELGIUM

(From Our Regular Correspondent)

Feb. 4, 1935.

Nephritis and Nephrosis

Prof. Polak Daniels has called attention to the difficulty of distinguishing, from the anatomopathologic point of view, the diseases that attack the epithelium of the renal tubules (nephrosis) and the disorders that provoke changes in the glomeruli (nephritis). Belle and McGregor hold, on the basis of histologic observations, that chronic lipoid nephrosis should be regarded as a special type of glomerulonephritis. If one seeks to superimpose the clinical picture of nephrosis and the anatomopathologic manifestations of this disease, it will soon be found that such superimposition is difficult, if not impossible.

The cardinal symptom of nephrosis is the edema. Can the typical anatomic lesion of nephrosis (cellular degeneration of the epitheium of the renal tubules) be considered responsible for the edema? If one takes account of the more recent views of renal physiology, the reply will be negative. It will be recalled that the glomeruli are ultrafilters and that the renal tubules are charged with the resorption of a part of the substance secreted by the glomeruli (concentration function). If the epithelium of the tubules is diseased, the resorption of the liquid will be impaired, and as a consequence diuresis will be increased. The edema associated with nephrosis cannot therefore be considered a direct consequence of the lesions found in the renal tubules. Daniels believes that it is much more logical to explain albuminuria as a glomerular lesion than as a degenerative lesion of the renal tubules.

Syphilis in Infants

At the ninth Congrès nationale des oeuvres de l'enfance, which was held at Tournai, it was decided, following a paper presented by Dr. Languy on "Syphilis in Infants: Diagnosis and Treatment," to apply all measures possible to intensify in Belgium the crusade against syphilis, which is an important factor in infant mortality. In this crusade there must be close and effective cooperation between the various organizations for detection, on the one hand (the prenatal consultation centers, the obstetric services, the consultation centers for infant care, and the centers of preventive medicine in general), and, on the other hand, between the organizations on which the treatment develops; namely, the whole medical profession of Belgium, aided in its task by the antivenereal dispensaries.

International Congress of Accidents and Occupational Diseases

The seventh Congrès international des accidents et des maladies du travail will be held at Brussels in July 1935, under the chairmanship of Dr. Glibert. The work of the congress will comprise official papers on the questions previously chosen for discussion:

Section A: Surgery

I. Remote results of traumatisms of the cranium: (*a*) etiology and symptomatology; (*b*) pathologic anatomy; (*c*) diagnosis, prognosis, evaluation and (*d*) treatment.

II. Traumatisms of the hand and the fingers: (*a*) immediate treatment of wounds of the hand and the fingers; (*b*) infectious complications of such wounds; (*c*) reparative operations after these traumatisms; (*d*) trophic and painful sequels; (*e*) estimation of disability caused by wounds of the hand and the fingers.

Section B: Occupational Diseases

I. The crusade against harmful dusts in industry: (*a*) how to secure and to examine dusts in order to determine their quality and quantity; (*b*) the relative value of the different means of combating industrial dusts suspended in the air; (*c*) criteria for the selection, before hiring, of workmen to be exposed to dangerous dusts; (*d*) the first alarming signs indicating an intolerance for a dangerous occupation.

II. The pathologic action of gases escaping from fire-damp veins. Does the repeated inhalation of minimal amounts of gases escaping from fire-damp veins exert a pathologic action? (*a*) the nature of fire-damp; its detection and prevention; (*b*) the physiologic and pathologic effects of fire-damp.

Section C: Miscellaneous

I. (*a*) psychophysiology of pain; (*b*) pathologic changes in the sense of pain; (*c*) objective diagnosis of pain in traumatized persons.

II. Electricity: (*a*) pathologic disorders due to electricity; (*b*) hygiene of electricity; (*c*) pathologic anatomy; (*d*) injuries due to electricity.

Osteitis of the Pubis

Addressing recently the Belgian Surgical Society, Drs. Jonckeere and Leclercq discussed the various forms of tuberculous osteitis occurring in the pubis. The two dominant factors in the evolution of osteotuberculosis of the pubis are the degree of gravity of the bone lesions and the stage (more or less advanced) of the abscess. They gave this therapeutic survey: 1. The nonsuppurative bone lesions may heal perfectly by the institution of a rational mobilization, combined with the general treatment of any tuberculosis. Unfortunately one seldom has an opportunity to apply such treatment, since tuberculous lesions of the pubis have at first a symptomatology that is obscure if not nonexistent. This method, however, should be borne in mind, for it may be advantageous to combine it with the surgical or orthopedic technic to which more serious clinical types are amenable. 2. Bone lesions with walled off collections require a different treatment, depending on whether or not there are sequestrums. The type without sequestrums, characteristic of diffuse or periosteal tuberculosis, should be subjected to modifying injections.

The typical form of circumscribed tuberculosis with sequestrums will necessitate a surgical intervention, which may be conservative or radical. If conservative, one will confine oneself to a curettage with removal of the pocket; in the second case one will undertake a symphyseal resection, which must be supplemented by an interpubic graft. 3. The bone lesions with fistulized collections constitute even to a greater extent a formal operative indication, consisting, as one may prefer, of a curettage or a pubic resection, either one of which will eliminate fistulous tracts.

Marriages

HELEN LA RUE WILLIAMS, Allentown, Pa., to Mr. Frank Hollingsworth Hodgens of Philadelphia, February 2.

DANIEL EARL KAVANAUGH to Miss Elizabeth Marion Current, both of Belleville, N. J., January 26.

LEO L. JACOBS, Richmond, Va., to Miss Esther Bloom of Covington, Ky., in Norfolk, February 14.

ALLEN W. BYRNES, Des Moines, Iowa, to Miss Elizabeth M. Early of Traer, Dec. 25, 1934.

JAMES S. MCELROY, Indianapolis, to Miss Katherine Dillin of Washington, Ind., February 2.

DEWITT T. BOND, Danielsville, Ga., to Miss Elsie Quattlebaum of Statesboro, recently.

JOHN FRANCIS HAMMOND to Miss Louise Sellergren, both of Chicago, February 24.

ROBERT M. HARBIN JR. to Miss Charlotte Dean, both of Rome, Ga., February 16.

GEORGE A. GRINDE, Cumberland, Wis., to Mrs. Helen Cole in December 1934.

WILLIAM J. MURPHY, Milwaukee, to Miss Vivian M. Dunn, Dec. 27, 1934.

Deaths

Jabez North Jackson ⊕ since 1932 director of health of Kansas City, Mo., died, March 18, aged 66. Dr. Jackson was born in Labadie, Mo., Oct. 6, 1868. After attending Central College in Fayette, Mo., where he received the bachelor of arts degree in 1889 and the master of arts degree in 1890, he graduated from the University Medical College of Kansas City in 1891, and later did graduate work at the New York Polyclinic. From 1891 to 1895 he was demonstrator of anatomy and from 1895 to 1898 professor of anatomy at his alma mater, professor of surgical anatomy and adjunct professor of surgery, 1898-1900, professor of principles and practice of surgery and clinical surgery, 1900-1911, trustee, 1891-1911, and at one time president. From 1893 to 1898 he was assistant surgeon and surgeon in the Third Regiment of the Missouri National Guard and was a major and brigade surgeon of the United States Volunteers in charge of the Second Division Hospital of the Second Army Corps during the Spanish-American War. Dr. Jackson was chosen President-Elect of the American Medical Association at the Dallas session in 1926, was President of the Association in 1927-1928 and was a member of the House of Delegates in 1903-1904, 1906, 1919, 1930-1931 and 1933. He was president of the Medical Association of the Southwest in 1898, of the Kansas City Academy of Medicine in 1900, of the Missouri State Medical Association in 1904, and of the Western Surgical Association in 1913. Among the other organizations of which he was a member were the American Surgical Association, the Missouri Valley Medical Society, the Pan-American Medical Congress and the American College of Surgeons. He was surgeon to the Kansas City General Hospital, the Research Hospital and the Trinity Hospital. He was awarded the doctor of science degree from Park College in 1926 and the doctor of laws from the University of Missouri in 1927.

John Ruhräh ⊕ Baltimore; College of Physicians and Surgeons of Baltimore, 1894; professor of pediatrics, University of Maryland School of Medicine; member and past president of the American Pediatric Society, the American Academy of Pediatrics and the Medical and Chirurgical Faculty of Maryland; past president and secretary-treasurer of the Medical Library Association; past president of the Research Society and the Osler Historical Society; visiting physician to the Mercy Hospital and the Hospital for Women of Maryland; consulting physician to the Church Home and Infirmary and the Bay View City Hospital; commissioner of public schools in Baltimore; co-author of "Diet in Health and Disease," "Dietetics for Nurses" and "Poliomyelitis"; author of "Manual of Diseases of Infants and Children" and "Pediatric Biographies"; editor of "Pediatrics of the Past," and "William Cadogan, His Essay on Gout"; associate editor of *Annals of Medical History;* contributed articles on "Pediatrics in Art" to the *American Journal of Diseases of Children;* aged 62; died, March 10, in the Mercy Hospital, of arteriosclerotic hypertensive cardiovascular disease and cerebral hemorrhage.

Ralph Walker McDowell ⊕ Medical Director, Captain, U. S. Navy, Washington, D. C.; Jefferson Medical College of Philadelphia, 1905; in 1934 Member of the House of Delegates of the American Medical Association; entered the navy as an assistant surgeon in 1908 and was promoted through the various grades to that of captain in 1931; was awarded the *Distinguished Service Medal* and was made a *Chevalier of the Legion of Honor of France* for service during the World War; professor of surgery at the U. S. Naval Medical School; chief of the surgical service at the U. S. Naval Hospital; consulting surgeon for the navy in the District of Columbia; fellow of the American College of Surgeons; formerly editor of the *Naval Medical Bulletin;* aged 52; died, February 22, of coronary thrombosis.

Robert Abrahams ⊕ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1891; formerly associate professor of medicine, New York Post-Graduate Medical School and Hospital; at various times on the staff of the Unity Hospital, Brooklyn, Rockaway Beach (N. Y.) Hospital and the Manhattan State Hospital; aged 73; died, March 2, of heart disease, at Pass-a-Grille, Fla.

Albert Bernheim, Philadelphia; Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg, Baden, Germany, 1890; University of Louisville (Ky.) Medical Department, 1897; member of the Medical Society of the State of Pennsylvania and the American Gastro-Enterological Association; aged 66; died, February 15, in the Jewish Hospital, of paralysis agitans and pneumonia.

Lucius Deyampert McGehee, Hammond, La.; Tulane University of Louisiana Medical Department, New Orleans, 1904; member of the Louisiana State Medical Society; past president of the Tangipahoa Parish Medical Society; for many years member of the parish school board; health officer of Hammond; aged 53; died, January 30, of pneumonia.

Frank William Stevens ⊕ Bridgeport, Conn.; Yale University School of Medicine, New Haven, 1900; fellow of the American College of Surgeons; served during the World War; for eleven years member of the board of health of Bridgeport; aged 61; on the staff of the Bridgeport Hospital, where he died, February 16, of carcinoma of the stomach.

Hubert Carlyle Dixon ⊕ Leaksville, N. C.; University and Bellevue Hospital Medical College, New York, 1916; fellow of the American College of Surgeons; past president of the Rockingham County Medical Society; served during the World War; on the staff of the Leaksville Hospital; aged 43; died, February 11, of coronary occlusion.

Andrew Joseph Sullivan ⊕ Brockton, Mass.; Tufts College Medical School, Boston, 1909; member of the New England Otological and Laryngological Society; fellow of the American College of Surgeons; served during the World War; on the staff of the Goddard Hospital; aged 49; died, February 9, of bronchiectasis and heart disease.

Mordecai Edward Doughty, Slocomb, Ala.; Chattanooga (Tenn.) Medical College, 1903; member of the Medical Association of the State of Alabama; formerly health officer of Slocomb, and county health officer; at one time member of the city council and board of education; aged 59; died, February 3, in a hospital at Dothan, of septicemia.

Walter Lewis Barber, Waterbury, Conn.; Bellevue Hospital Medical College, New York, 1873; member of the Connecticut State Medical Society; for many years member of the state board of medical examiners and city board of health; on the staff of the Waterbury Hospital; aged 83; died, February 14, of cerebral hemorrhage.

John William Foley, Denver; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1894; member of the American Academy of Ophthalmology and Otolaryngology; served during the World War; aged 61; died, February 17, in the Fitzsimons General Hospital, of cerebral hemorrhage.

Louis Andrew King, St. Joseph, Mich.; Saginaw (Mich.) Valley Medical College, 1903; member of the Michigan State Medical Society; served during the World War; formerly mayor of St. Joseph; on the staff of the Mercy Hospital, Benton Harbor; aged 65; died, February 1, of cerebral hemorrhage.

Foster Victor Brown, Sioux City, Iowa; Sioux City College of Medicine, 1905; member of the Iowa State Medical Society; past president and secretary of the Woodbury County Medical Society; on the staffs of the Lutheran and Methodist hospitals; aged 56; died, February 12, of cirrhosis of the liver.

Lee Jones, Blount Springs, Ala.; University of Virginia Department of Medicine, Charlottesville, 1909; served during the World War; for many years on the staffs of the Goldsby King Memorial Hospital and the Selma Baptist Hospital, Selma; aged 53; died, January 11, of heart disease.

Lawrence G. Clayton, Central, S. C.; University of Maryland School of Medicine, Baltimore, 1878; member of the South Carolina Medical Association; past president of the Pickens County Medical Society; aged 80; died, February 17, of bronchopneumonia and acute dilatation of the heart.

James Edward Terry, Red Level, Ala.; University of Alabama Medical Department, Mobile, 1902; member of the Medical Association of the State of Alabama; chairman of the school board; aged 59; died, February 5, in St. Margaret's Hospital, Montgomery, of strangulated umbilical hernia.

John H. Samuel, Maysville, Ky.; Medical College of Ohio, Cincinnati, 1877; mayor of Maysville, 1920-1924; formerly member of the state board of health and president of board of education; aged 79; died, February 18, of pneumonia following an operation for intestinal obstruction.

Harry Blatt Harris, Orange, N. J.; Columbia University College of Physicians and Surgeons, New York, 1906; member of the Medical Society of New Jersey; health officer of Orange; aged 50; died, February 12, in the Beth Israel Hospital, Newark, of uremia, nephritis and heart disease.

Horace Elwood Bragdon, Winthrop, Mass.; Harvard University Medical School, Boston, 1891; member of the Massachusetts Medical Society; for twenty years on the staff of the Chelsea (Mass.) Memorial Hospital; aged 67; died, February 17, of coronary thrombosis.

Edmund A. Christian ✠ Pontiac, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1882; member of the American Psychiatric Association; aged 77; medical superintendent of the Pontiac State Hospital, where he died, February 5, of heart disease.

Robert M. Kendrick, Selmer, Tenn.; St. Louis College of Physicians and Surgeons, 1897; member of the Tennessee State Medical Association; formerly a druggist; for many years bank president and chairman of the school board; aged 64; died, February 20, of pneumonia.

John Hamilton Small, Montclair, N. J.; Medico-Chirurgical College of Philadelphia, 1902; formerly assistant, adjunct and associate professor of bacteriology at his alma mater; aged 69; died, February 23, in the Memorial Hospital, Miami, Fla., of diabetes mellitus and carbuncle.

Oscar Suttle Justice, Central, Ala.; Medical College of Alabama, Mobile, 1885; member of the Medical Association of the State of Alabama; formerly member of the state legislature; at one time county health officer; aged 74; died, February 10, of cerebral hemorrhage.

Horace Lee Simpson, Pensacola, Fla.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1886; member of the Florida Medical Association; on the staff of the Pensacola Hospital; aged 71; died, February 4, of cerebral hemorrhage.

Stephen Livingston Taylor ✠ Sherrill, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1894; for many years health officer of Sherrill; aged 66; died, January 29, in the Faulkner Hospital, Boston, of heart disease.

William T. Short, Stonington, Ill.; Marion-Sims College of Medicine, St. Louis, 1897; member of the Illinois State Medical Society; formerly district health superintendent of the state department of health; aged 62; died, February 10, of acute dilatation of the heart.

Frederick Jacob Korthals, Milwaukee; Marquette University School of Medicine, Milwaukee, 1914; member of the State Medical Society of Wisconsin; served during the World War; on the staff of St. Joseph's Hospital; aged 46; died, February 4, of colitis.

George Wallace Rawson, Amherst, Mass.; Dartmouth Medical School, Hanover, N. H., 1888; member of the Massachusetts Medical Society; member of the school board; aged 73; died, Dec. 26, 1934, of carcinoma of the stomach, myocarditis and arteriosclerosis.

Earl Gates Heaton, Baldwinsville, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1896; bank president; formerly village president and member of the board of education; aged 60; died, February 7, of coronary occlusion and arteriosclerosis.

Alvah Arlington Fisher, Providence, R. I.; University of the South Medical Department, Sewanee, Tenn., 1895; member of the Rhode Island Medical Society; served during the World War; aged 63; died, February 15, in the Rhode Island Hospital, of leukemia.

Frank Eugene Guild ✠ Willimantic, Conn.; Long Island College Hospital, Brooklyn, 1885; on the staff of the Windham Community Memorial Hospital; aged 81; died, February 3, in the Johns Hopkins Hospital, Baltimore, of infection of the urinary tract.

Francis Adams McClintock, Newcomb, Tenn.; Tennessee Medical College, Knoxville, 1895; member of the Tennessee State Medical Association; secretary and past president of the Campbell County Medical Society; aged 73; died, February 18, of pneumonia.

Barney Ferrell, Bend, Ore.; Northwestern University Medical School, Chicago, 1904; veteran of the Spanish-American War; on the staffs of the Lumbermen's and St. Charles hospitals; aged 59; died, January 15, of pulmonary tuberculosis.

Henry Holliday Stromberger, Los Angeles; Columbian University Medical Department, Washington, D. C., 1899; aged 68; died, February 1, in the Santa Monica (Calif.) Hospital, of a skull fracture received when he was struck by an automobile.

Lawrence Edward Zuley ✠ Oak Park, Ill.; Loyola University School of Medicine, Chicago, 1932; on the staffs of the West Suburban Hospital and the Oak Park Hospital; aged 28; died, February 14, of appendicitis, general peritonitis and pneumonia.

De Witt Clinton Wilson, Los Angeles; Bellevue Hospital Medical College, New York, 1870; formerly member of the state legislature of Ohio, member of the city council and school board of Ironton, Ohio; aged 87; died, February 1, of cystitis.

Samuel Corley Ball, Fort Worth, Texas; Kentucky School of Medicine, Louisville, 1887; member of the State Medical Association of Texas; served during the World War; aged 69; died, January 23, in Texarkana, of hypertensive heart disease.

William Timothy Cannon, Brooklyn; Baltimore Medical College, 1901; formerly resident physician in the Brooklyn Home for Consumptives; aged 59; died, January 19, in the Swedish Hospital, of heart disease, following an operation.

George Hartnagel, Delphos, Ohio; Northwestern University Medical School, Chicago, 1910; member of the Ohio State Medical Association; served during the World War; aged 55; died, February 8, of acute coronary occlusion with infarct.

Walter S. Zorns, Taylor, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1920; member of the State Medical Association of Texas; health officer of Taylor; aged 43; died, February 22, of acute lymphatic leukemia.

William Andrew Crooks ✠ Wahjamega, Mich.; Hahnemann Medical College and Hospital, Chicago, 1899; formerly medical superintendent of the Michigan Farm Colony for Epileptics; aged 62; died, February 5, of carcinoma.

William David Tyrrell ✠ New York; Northwestern University Medical School, Chicago, 1899; on the staff of the Willard Parker Hospital; aged 64; died, February 26, when he fell from a nine story window of a hospital.

William Jennings Bauer, Indianapolis; State University of Iowa College of Medicine, Iowa City, 1933; aged 38; resident physician to the Methodist Episcopal Hospital, where he died, February 8, of subacute bacterial endocarditis.

Frank Scott Campbell, State College, Pa.; Medico-Chirurgical College of Philadelphia, 1896; member of the Medical Society of the State of Pennsylvania; aged 66; died, February 12, of cardiovascular renal disease.

Augustus Oreline, New York; Julius-Maximilians-Universität Medizinische Fakultät, Wurzburg, Bavaria, Germany, 1886; aged 72; died recently, in the Lenox Hill Hospital, of hypertrophy of the prostate and uremia.

Moses Gatlin Campbell, Atlanta, Ga.; Atlanta Medical College, 1894; an Affiliate Fellow of the American Medical Association; on the staff of the Georgia Baptist Hospital; aged 73; died, February 8, of heart disease.

Millard Lafayette Stephens, Haleyville, Ala.; Birmingham Medical College, 1909; member of the Medical Association of the State of Alabama; formerly mayor of Haleyville; aged 52; died, February 1, of pneumonia.

William M. Finley, Blountsville, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1879; aged 77; died, January 24, in a hospital at Birmingham, of chronic myocarditis and hypertrophy of the prostate.

William E. Fisher, Portland, Conn.; University of Pennsylvania Department of Medicine, Philadelphia, 1876; member of the Connecticut State Medical Society; aged 81; died, recently, of chronic myocarditis.

Samuel G. Miller, Chester, S. C.; College of Physicians and Surgeons, Baltimore, 1879; member of the South Carolina Medical Association; aged 74; died, January 21, of arteriosclerosis and senile gangrene.

Antonino Scaturro ✠ New York; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1899; on the staff of the Columbus Hospital; aged 59; died, February 6, of a self-inflicted bullet wound.

Hugh Smith Rowlett, Maryville, Mo.; Louisville (Ky.) Medical College, 1894; served during the World War; on the staff of St. Francis Hospital; aged 65; died, February 18, of arteriosclerosis and uremia.

Bernard Miller, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; aged 58; died, February 13, of angina pectoris and chronic myocarditis.

Melvin William Lilly, Grandview, Iowa; State University of Iowa College of Medicine, Iowa City, 1872; formerly member of the board of health of Chicago; aged 84; died, February 6, of heart disease.

Marion A. McClelland ✠ Aguilar, Colo.; St. Louis College of Physicians and Surgeons, 1926; served during the World War; aged 39; died, February 18, in St. Mary's Hospital, Pueblo, of pneumonia.

William H. Clegg, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1891; aged 69; died, January 30, in the Philadelphia General Hospital, of carcinoma of the prostate.

William S. Aldridge, Lake Worth, Fla.; Western Reserve University Medical Department, Cleveland, 1892; formerly health officer and city physician; aged 68; died, February 9, of heart disease.

Leslie James Lynch, Columbus, Ohio; College of Physicians and Surgeons, Keokuk, Iowa, 1879; also a druggist; aged 86; died, February 13, at the Grant Hospital, of cerebral hemorrhage.

Samuel A. Poague, Clinton, Mo.; Marion-Sims College of Medicine, St. Louis, 1892; member of the Missouri State Medical Association; aged 69; died, February 17, of senile dementia.

Thomas Benton Selman, Silsbee, Texas; Atlanta (Ga.) Medical College, 1890; member of the State Medical Association of Texas; aged 79; died, February 1, of pellagra and senile dementia.

Willis S. Michael, Junior, W. Va.; College of Physicians and Surgeons, Baltimore, 1893; member of the West Virginia State Medical Association; aged 63; died recently, of angina pectoris.

Frederick Huber Brumm, Coldwater, Ohio; Medical College of Ohio, Cincinnati, 1907; member of the Ohio State Medical Association; aged 50; died, February 10, of heart disease.

Rush Kersey Morton, Juniata Pines, N. J.; College of Physicians and Surgeons, Baltimore, 1900; veteran of the Spanish-American War; aged 72; died, January 10, of heart disease.

Jesse S. Driver, Coolidge, Texas; Memphis (Tenn.) Hospital Medical College, 1891; member of the State Medical Association of Texas; aged 68; died, January 18, of tuberculosis.

Marie Burnadette Lucas, Washington, D. C.; Howard University College of Medicine, Washington, 1914; aged 60; died, February 23, of purpura haemorrhagica and pulmonary edema.

Fred Bowers Taylor, Concord, N. H.; Tufts College Medical School, Boston, 1909; member of the New Hampshire Medical Society; aged 53; died, January 24, of cerebral hemorrhage.

William L. Bowers, Vada, Ga.; Chattanooga (Tenn.) Medical College, 1899; member of the Medical Association of Georgia; aged 68; died, February 8, of cerebral hemorrhage.

Charles Fleet Scudder, Northport, N. Y.; Cornell University Medical College, New York, 1911; served during the World War; aged 49; died, February 3, of heart disease.

William Beardsley Wilkinson, Staten Island, N. Y.; Bellevue Hospital Medical College, 1896; aged 66; died, February 2, in the Staten Island Hospital, of lobar pneumonia.

Charles F. Adams, Springfield, Ohio; Medical College of Ohio, Cincinnati, 1884; member of the Ohio State Medical Association; aged 73; died, February 15, of heart disease.

Spurgeon Campbell, Winnipeg, Manit., Canada; Manitoba Medical College, Winnipeg, 1904; served during the World War; aged 64; died, February 10, of coronary thrombosis.

James N. Downs, Atkinson, Ill.; Homeopathic Hospital College, Cleveland, 1880; member of the Illinois State Medical Society; aged 80; died, February 3, of coronary occlusion.

William Beringer Marcusson, Oak Park, Ill.; Rush Medical College, Chicago, 1885; aged 74; died, February 17, of cerebral arteriosclerosis, thrombosis and pneumonia.

James T. Gibson ✠ Lynchburg, Ohio; Medical College of Ohio, Cincinnati, 1897; member of the board of education; aged 66; died, February 14, of heart disease.

John Inman Smith, London, Ky.; Hospital College of Medicine, Louisville, 1892; served during the World War; aged 68; died, February 17, of heart disease.

Oran D. McCray, Marshall, Mo.; University Medical College of Kansas City, 1901; aged 58; died, Dec. 12, 1934, of carcinoma of the liver and diabetes mellitus.

Frederick Tracy Fitch ✠ East Hampton, Conn.; Yale University School of Medicine, New Haven, 1904; aged 57; died suddenly, February 16, of heart disease.

Richard Henry Houghton, Boston; Tufts College Medical School, Boston, 1905; aged 58; died, February 8, in the Peter Bent Brigham Hospital, of arteriosclerosis.

William Henry Foster, St. Louis; St. Louis University School of Medicine, 1905; aged 59; died, February 9, in the Missouri Baptist Sanitarium, of pneumonia.

John Wilford Stiers, Detroit; Northwestern University Medical School, Chicago, 1914; served during the World War; aged 45; died, February 10, of pneumonia.

Harley Heath ✠ Comstock, N. Y.; Albany Medical College, 1909; chief physician to the Great Meadow Prison; aged 54; died, February 12, of heart disease.

August Blass Lacour, Batchelor, Ia.; Memphis (Tenn.) Hospital Medical College, 1909; aged 53; died, February 2, of heart disease and cerebral hemorrhage.

Marcus Warland Laney, Birmingham, Ala.; Vanderbilt University School of Medicine, 1893; aged 71; died, February 5, of cerebral hemorrhage following a fall.

Perry Edgar Mitchell, Wetumka, Okla.; University of Nashville (Tenn.) Medical Department, 1905; aged 54; died, February 16, of cerebral hemorrhage.

Casper M. Droste, Grand Rapids, Mich.; College of Physicians and Surgeons of Chicago, 1885; aged 73; died, February 16, of heart disease, in St. Louis.

David M. Bonham, Crawfordsville, Ind.; Eclectic Medical Institute, Cincinnati, 1875; aged 86; died, February 15, of carcinoma of the mouth and throat.

William Clinton Seitz, Glen Rock, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1888; aged 70; died, February 4, of cerebral hemorrhage.

Vincent Gialloreti, Chicago; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1892; aged 69; died, March 6, of cerebral hemorrhage.

William A. Coldren, Uhrichsville, Ohio; University of Pennsylvania Department of Medicine, 1888; aged 75; died, February 9, of diabetes mellitus.

Sarah Alice Cohen May, New York; Woman's Medical College of Pennsylvania, Philadelphia, 1879; aged 74; died, Dec. 10, 1934, of arteriosclerosis.

Levi Willard Clough, Charlestown, N. H.; University of Vermont College of Medicine, Burlington, 1887; aged 71; died, February 5, of arteriosclerosis.

George Francis Goggins, De Pere, Wis.; Marquette University School of Medicine, Milwaukee, 1913; aged 49; died, February 16, of heart disease.

Royal Woods, Omaha; Rush Medical College, Chicago, 1889; served during the World War; aged 70; died, January 24, of carcinoma of the stomach.

Joseph M. Page, Dublin, Ga.; University of Georgia Medical Department, Augusta, 1883; aged 74; died, Dec. 14, 1934, of cerebral hemorrhage.

Joseph B. McClure, Norman, Okla.; Hospital College of Medicine, Louisville, Ky., 1894; aged 72; died, in February, of coronary thrombosis.

Walter Joseph Downs, Alfred, Maine; Medical School of Maine, Portland, 1883; aged 79; died, Dec. 14, 1934, of cerebral hemorrhage and pyelitis.

Ellis Corwin Cope ✠ Barton, Ohio; Ohio Medical University, Columbus, 1893; aged 65; died, February 13, of erythema multiforme and uremia.

Anson S. Beckwith, London, Ohio (licensed in Ohio in 1896); aged 70; died, February 20, in a hospital at Columbus, of arteriosclerosis.

Robert Wiener ✠ New York; Eclectic Medical College of the City of New York, 1901; aged 58; died, January 1, of angina pectoris.

Isabel Livingston, Needham, Mass.; College of Physicians and Surgeons, Boston, 1903; aged 82; died, February 4, of carcinoma.

Solomon Elswit, New York; Long Island College Hospital, Brooklyn, 1904; aged 52; died, Dec. 27, 1934, of heart disease.

Lee H. Tully ✠ Evansville, Ind.; Louisville (Ky.) Medical College, 1890; aged 65; died, February 21, of asthma and heart disease.

H. V. Copenhaver, Rock Island, Tenn. (licensed in Tennessee in 1904); aged 72; died, January 29, of a malignant tumor.

Homer M. Calvin, Salineville, Ohio; Columbus Medical College, 1891; aged 67; died, February 3, of carcinoma of the liver.

Robert M. Funkhouser, Fairfield, Ill. (licensed in Illinois in 1879); aged 84; died, February 1, of arteriosclerosis.

Correspondence

PHOTOGRAPHS OF DR. WILLIAM H. WELCH

To the Editor:—It is proposed to print an iconography of the best extant photographs of the late Dr. William H. Welch at different periods of his life, as a joint publication of the Institute of the History of Medicine and of the Welch Medical Library, Baltimore. A large number of such pictures have been assembled from his estate and otherwise, but there are undoubtedly various snap shots taken by various hands of which we have no knowledge. If copies of these can be mailed to the undersigned, it will be much appreciated by those interested in the matter and due acknowledgment will be given whenever such pictures can be used.

F. H. GARRISON, M.D.,
1900 East Monument Street,
Baltimore.
Librarian, Welch Medical Library.

DISTINGUISHING B. COLI AND AEROGENES TYPES

To the Editor:—Since Dr. A. M. Crance believes it very important to distinguish between B. coli and "aerogenes types" in treating cases of bacilluria (THE JOURNAL, January 26, p. 285), I should like to point out an error in his method of differentiating these two species. Dr. Crance states that "Aerogenes produces gas within forty-eight hours in saccharose, whereas Escherichia does not." Bacteriologists have long recognized saccharose and nonsaccharose fermenting strains of B. coli and have termed them B. coli-communior and B. coli-communis, respectively. Thus Dr. Crance's test does not distinguish B. coli-communior from B. aerogenes. The importance of this distinction becomes apparent when it is realized, as Jordan (ed. 10, 1931) states that "nearly one half of the colon bacilli that are isolated from various sources produce gas in saccharose broth." It is surprising that Dr. Crance does not use the well recognized methods for differentiating these two groups, such as the methyl red, Voges-Proskauer, uric acid or citrate tests. Regarding the rationale on which Dr. Crance bases his "four-point treatment," it appears that the treatment contains several mutually counteracting procedures. The difficulty with which B. acidophilus is established and maintained in the colon is well known and it therefore seems rather useless to try to implant this organism by feeding while at the same time the colon is being washed out daily with enemas (for the purpose of removing B. coli but presumably not B. acidophilus). It is also recognized that a diet containing milk and lactose is essential for implanting B. acidophilus in the colon, yet Dr. Crance's treatment consists of "two weeks of high protein diet, two weeks of high fat diet, and two weeks of high carbohydrate," and "the daily use of a good acidophilus preparation, preferably not in milk."

THOMAS C. GRUBB, PH.D., Brooklyn.

[This letter was referred to Dr. A. M. Crance, who replies:]

To the Editor:—For clinical and practical reasons it is less confusing if such terminology as B. communis and B. communior is omitted. The former should be termed Escherichia coli. The latter, or the communior, is one of the saccharose fermenting strains and, clinically speaking, may be treated the same as B. aerogenes. Two methods are applicable in distinguishing B. aerogenes from B. communior. The indole test is positive for the communior, negative for the aerogenes. The Voges-Proskauer test is positive for the aerogenes, negative in the case of the communior. Neither of these tests, however, is necessary in distinguishing Escherichia coli from B. aerogenes. On referring to the Bergey Manual of Bacteriological Classification, one will find some seven or eight varieties of aerogenes and twenty-two varieties of Escherichia. Certainly one cannot expect to subdivide the groups to any such extent as this. There will be much less confusion if the two major types of Escherichia coli and Aerobacter aerogenes remain as the outstanding ones so far as clinical treatment is concerned. These two organisms are decidedly different in their clinical management. Work is now being carried out in order to determine whether there is any difference in the effect of certain methods of therapy as applied to the aerogenes and the communior. For practical reasons it seems best, for the present at least, to treat these two types as one and the same organism, although it is definitely known that they differ somewhat bacteriologically.

Regarding the rationale of the "four-point treatment," experience has shown that the results have been satisfactory. The effect of acidophilus is perhaps accomplished before it reaches the colon, and certainly these organisms continue to pour into the colon from higher up in the intestinal tract, regardless of the daily enemas.

In answer to the necessity of milk with acidophilus, the very fact that it has been successfully marketed in solution of pure whey, remaining culturally active, should be sufficient evidence that its presence in milk is not essential to its existence.

A. M. CRANCE, M.D., Geneva, N. Y.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

TESTS OF SYMPATHETIC NERVOUS SYSTEM

To the Editor:—I am interested in knowing how to diagnose paralysis of the sympathetic nervous system in which there is involvement of the peripheral structures, as the skin and blood vessels. How frequently are these structures affected in poliomyelitis? Please omit name.

M.D., New York.

ANSWER.—The methods of diagnosing lesions of the sympathetic nervous system in which there is involvement of peripheral structures include such tests as the histamine test, nerve blocking test and Brown fever test.

These structures are frequently affected in anterior poliomyelitis.

Operations have been performed on the sympathetic nervous system by Royle and Hunter, Davis, Pollock, Adson, Wade, and Morton and Scott.

The term "sympathetic" was introduced by Winslow in 1732. The autonomic nervous system is regarded as the division of the nervous system that includes all the neurons lying outside the central nervous system and cerebral spinal ganglions except those associated with the special sense organs.

Owing to the fact that the sympathetic nervous system serves as a connecting link between the spinal cord and the internal organs, peripheral blood vessels, erector muscles of the hair and sweat glands, which connection is accomplished by means of the ramicommunicantes, various tests have been made to determine its physiology and its lesions.

In the Landis test the forearm of the patient is immersed in water at a temperature of from 43 to 45 C. for thirty-five minutes, which produces vasodilatation in the lower extremities. If the surface temperature of the toes rises above 36.5 C., significant obliterative structural disease of the arteries of the lower extremities is definitely absent. If the surface temperature fails to rise to this level, organic arterial obstruction is probably present. These results correspond fairly accurately with the results observed after intravenous injection of typhoid vaccine used in spinal anesthesia and anesthetization of the posterior tibial nerve.

In the vasomotor index of Brown, fever is induced with intravenous typhoid vaccine and the increase of surface temperature of the limb is measured at half hour intervals with a thermocouple galvanometer.

In the histamine test, a small area of skin on the wrist, ankle or knee is cleansed with alcohol, which is allowed to dry. A drop of 1:1,000 solution of histamine phosphate is placed on it and introduced into the epidermis by multiple needle punctures in a manner similar to that used for cowpox vaccination. The excess histamine is gently removed. The characteristic response is thus described by Caldwell and Mayo: 1. A reddish purple spot appears as the result of local capillary dilatation. 2. A local wheal succeeds, because of transudation of serum from increased permeability of the capillaries. 3. A flair results as the effect of dilatation of the arteries by the reflex of a local axon.

White suggested procaine block of the sympathetic nerve on the upper or lower extremities by paravertebral injection to the first and second thoracic sympathetic ganglions if the upper extremities are being tested. Following the successful block, the rise in skin temperature is identical with the rise occurring after sympathetic ganglionectomy, as the temporary block creates conditions identical with those following the operation. It also imitates the effect of the operation in that pain of sympathetic origin will disappear and thus demonstrate what can be expected from the operation.

White, and especially Morton, advocate spinal anesthesia to determine whether there is a vascular spasm and occlusion of the lumen or whether a combination of the two exists. Spinal anesthesia blocks all motor sensory and sympathetic impulses and permits a maximal vascular dilatation. The vasomotor fibers to the blood vessels run in the peripheral nerves and are given off to the blood vessels segmentally. A block of the peripheral nerve should result in an increase in temperature of the innervated limb, because, together with motor and sensory nerves, the vasoconstrictors also will be paralyzed.

In describing the block of the brachial plexus, de Takáts pointed out the hyperemia and rise in temperature of the arm that appears during a successful anesthesia.

The investigations of Royle and Hunter have opened up a relatively new field for surgical exploration. Some of the indications of sympathetic disturbances are Horner syndrome in the eye, circulatory disturbances of the extremities, arthritis, Hirschsprung's disease and spasticity of muscle.

According to Flothow it is on anatomic and functional knowledge that sympathetic surgery in the following lesions has been based: (1) Raynaud's disease; (2) thrombo-angiitis obliterans; (3) generalized scleroderma; (4) Hirschsprung's disease and chronic constipation; (5) spastic paraplegia; (6) chronic arthritis.

According to Craig, surgery of the sympathetic nervous system has proved of extreme value in relieving the symptoms in diseases that are associated with hyperactivity of the vasoconstrictor influence on the muscles producing cold, clammy extremities.

The majority of patients with Raynaud's disease are immediately relieved from their symptoms following this operation. Certain selected cases of thrombo-angiitis obliterans and chronic infectious arthritis are relieved in direct ratio in amount to the associated vasoconstriction present in the vessels of the extremities. Certain diseases of the colon and bladder are relieved also by interruption of the sympathetic nerve supply.

Diagnostic injection of the sympathetics may be used to determine the proper level for amputation when this operation is necessary, and the injection of alcohol will permit a low point of amputation and secure better healing of the stump.

Periarterial sympathectomy consists essentially in removing the adventitia with the nerve plexus contained in it from a segment of the vessel several centimeters in length.

Doppler proposed painting the femoral artery with a 7 per cent solution of phenol, thereby damaging the highly vulnerable fibers of the sympathetic nerves causing a marked vasodilatation. It is said to be simpler than the Leriche periarterial sympathectomy.

The following references give further details:

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Brown, G. E., and Adson, A. W.: Calorimetric Studies of the Extremities Following Lumbar Sympathetic Ramisection and Ganglionectomy, *Am. J. M. Sc.* **170:** 232 (Aug.) 1925.
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DERMATITIS HERPETIFORMIS

To the Editor:—A boy, aged 12, otherwise healthy and normal, was stung or bitten by insects two years ago while the family was camping in the woods of Ontario. The insects appeared to be mosquitoes but the lesions have healed and recurred at intervals ever since. An intense itching and swelling results with a small central vesicle or pustule, which is ruptured and serum exudes for a time and then heals for a while, leaving very little evidence or mark, to recur again. All the lesions are on the legs and arms. The parents took him to a physician, who pronounced it the result of wood tick bites. His treatment, however, gave no relief and two or three crops have annoyed the patient for the past year.

W. P. LONG, M.D., Weatherly, Pa.

ANSWER.—An intensely itching recurrent vesicular and pustular eruption is most probably dermatitis herpetiformis. The wheals of urticaria rarely become vesicular, and a disease characterized by the recurrence of lesions that are consistently vesicular is not urticaria. While the distribution is not characteristic for dermatitis herpetiformis and nothing is said of grouped lesions, the disease in children is frequently atypical.

Whether the insect bites have any etiologic importance is a question. Dermatitis herpetiformis sometimes follows infection and in children frequently follows vaccination. The supposed insect bites may have been the first lesions of the disease.

A patch test made with a 50 per cent ointment of potassium iodide should bring out the eruption. Iodides given internally in full doses sometimes cause an exacerbation.

Arsenic internally, usually as solution of potassium arsenite, in full dose usually clears up the eruption temporarily and abates the itching. Prescriptions should always bear the warning "not to be refilled," for the use of arsenic should always be under the control of the physician. Likewise roentgen rays in one-fourth erythema dose (75 roentgens) once a week may clear up the eruption; but they too may be harmful if carried beyond the sum of two erythema doses (600 roentgens) on any one area of the skin, no matter how long the interval is between doses.

The rules of hygiene, with regularity of sleep, exercise and food, should be observed. Coffee, tea, cocoa, coca cola or anything conducive to nervousness should be avoided. Focal infections should be eradicated if found, and vaccines made from organisms isolated from these sources may be used. The stools should be examined for parasites.

Ultraviolet rays in a first degree erythema dose benefit some patients and when used over a long period may result in cure. Autogenous blood, from 5 to 10 cc. in a boy of 12 years, may be given intramuscularly every fifth day with great benefit in some cases.

Desiccated thyroid, iodides in small dosage, antipyrine, acetanilid, emetine in cases presenting pyorrhea, and salicin have all been credited with cures. Opening the vesicles may relieve the itching; sulphur baths, 60 Gm. of sulphurated potash to the bath, or sulphur in ointment may give temporary relief.

PRURITUS OF SCROTUM

To the Editor:—I have a patient with a subjective pruritus located on the scrotum which attacks with intense ferocity on one side or the other, rarely on the two sides at the same time. He has received a great deal of treatment, including x-rays, radium, even extirpation of a certain itchy area, and the eradication of a varicocele. A very careful study fails to reveal any pathologic lead on which one could go ahead, with the exception that about ten years ago he had gonorrhea, received treatment and made an apparently uneventful recovery. The Wassermann reaction is negative. Please omit name.

M.D., Massachusetts.

ANSWER.—It is assumed from the description that the skin of the scrotum is normal. The case is therefore one of the fortunately rare ones of essential pruritus—a nervous ailment.

It is important that general and local hygienic measures be followed strictly. Coffee, tea, condiments, hot foods, alcohol and tobacco should be forbidden or at least limited as much as possible. Regularity of habits must be insisted on, a generous amount of water ingested, and whatever necessary done to insure adequate elimination by the bowels. Sleep must be secured if necessary by drugs—preferably bromides, chloral and cannabis, with care to avoid habit formation. Morphine and opium are to be avoided both because of the danger of habituation and because they are often harmful, actually increasing the itching.

The skin must be protected from the maceration of sweat by gentle washing with a sodium bicarbonate solution, dabbed

dry and abundantly powdered. If necessary, flat gauze powder bags may be suspended between the scrotum and the thighs. If the skin is dry, soap should be avoided and cleansing done with oil. The habit of rubbing and scratching must be avoided, for this by itself can keep up the itching. Rough clothing must also be avoided.

A tragacanth lotion containing phenol (not over 0.5 per cent), menthol and camphor or chloral hydrate may be helpful. Potassium permanganate solution 2 per cent may be painted on the skin daily, or silver nitrate solution up to 10 per cent, changing to a bland ointment when fissuring occurs.

C. G. Andrews (Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1930, p. 367) speaks well of the results of alcohol injection into the skin. After surgical preparation, 95 per cent alcohol may be injected into the skin with a hypodermic syringe under general anesthesia. The needle is directed perpendicularly to the skin surface and 0.15 cc. (2 or 3 minims) of alcohol deposited just beneath the skin. These injections are spaced about 0.6 cm. (one-fourth inch) apart over the whole itchy area. No dressing is necessary. This does away with itching for six months or more, when the pruritus may recur, usually less intensely. The treatment may then be repeated if necessary.

TOXEMIA DURING POLLEN THERAPY

To the Editor:—During the past summer I administered a complete series of injections of pollen extract (ragweed and related genera) to a woman, aged 37, and her son, aged 10 years. The prophylaxis against hay fever was entirely satisfactory. However, both patients claim that they have been rendered exceedingly nervous as a result of these treatments. In the woman, this is said to manifest itself as inability to concentrate, impairment of memory, and a tendency to shun the society of other people. There is also said to be a feeling of trembling throughout the body. In the boy there is said to be an inability to grasp his lessons at school or to advance in his study of the piano. In regard to the mother, there seems to be no evidence that she is going through the menopause. There has been no basal metabolism test to rule out hyperthyroidism, but such signs as rapid pulse, tremor of the hands and the various ocular symptoms cannot be elicited. The patient states that she is acquainted with several other persons who have been affected in a similar manner by these treatments. In these two patients there were no disagreeable reactions following any of the injections. Do you have any information at hand that would suggest whether or not there is any frequent effect on the nervous system following these injections? Kindly omit name.

M.D., Ohio.

ANSWER.—Occasionally a form of toxemia may occur during the course of pollen therapy. The patient may complain of general lassitude, lack of appetite and loss of weight. The symptomatology described by the inquirer has never been seen in the course of the care of many hundreds of hay fever patients, nor does the literature contain any clear-cut examples of it. The occurrence of the same clinical picture in both the mother and child should make one highly suspicious of a psychoneurosis. The further fact that the patient claims that she knows of several other acquaintances who are similarly affected by pollen treatments should cause one to be even more than suspicious of her mental state.

This opinion takes into consideration the following possible exceptions: A disturbance of the nervous system may result in consequence of repeated and frequent systemic reactions. The use of ephedrine or ephedrine-like preparations along with the pollen therapy may result in symptoms as described. If these conditions do not prevail, the patients may be considered psychoneurotic and it may be well to cease treatment because of the unstable mental state and because of the possibility of development of an even greater variety of symptoms of psychogenic origin.

INTERMITTENT CLAUDICATION

To the Editor:—Will you please tell me the most recent explanation for the cause of pain in the leg of a patient with intermittent claudication? Should carbohydrates be restricted in such a case? Has insulin been used with benefit? What treatment is most beneficial? What is the prognosis in a case with onset one year ago at the age of 61? The general health of this patient has been good in other respects. Please omit name and address.

M.D., Ohio.

ANSWER.—If the patient has claudication, it is attributable solely to obstruction of the main arteries of the affected extremity. If the claudication is in the calf muscles, closure includes levels as high as the popliteal artery. The pain of claudication results from an insufficient amount of arterial blood reaching an actively exercising muscle. Relief is always obtained by rest, and a definite amount of exercise always will bring on the distress in the same situation. The symptom always means that there is an obstructive lesion in the major arteries of the affected extremity.

Dietetic treatment is of no avail. Insulin has no effect on claudication. The most efficacious treatment known at the present time is the use of tissue extracts. There are various types of tissue extract: that prepared from the pancreas (insulin free), and that prepared from heart or skeletal muscle. They all contain some substance that apparently affects the metabolism of actively exercising muscle that is receiving a deficient supply of arterial blood. Pancreatic tissue extract, given by intramuscular injections of from 3 to 5 cc., usually increases the exercise tolerance several fold. Administration can be repeated at varying intervals, depending on how long the beneficial effects last. Of equal importance, if the peripheral arteries are obstructed, is extreme care of the feet to avoid the development of ulcers or gangrene.

HEADACHES DURING MENSTRUATION

To the Editor:—Is there any treatment to prevent headaches and nervous upsets associated with the menses when during two pregnancies the symptoms were entirely relieved? Please omit name.

M.D., California.

ANSWER.—In pregnant women, many changes occur throughout the course of gestation. Among these alterations are an increased production and excretion of estrogenic substance and gonad-stimulating principle. R. T. Frank has shown that in the great majority of normal nonpregnant women there is little follicular hormone in the circulating blood until the seventh day before the onset of the menstrual bleeding. At this time there is an abrupt rise in the amount of hormone but immediately after the onset of the menses a precipitous fall in the quantity of hormone regularly takes place. Hence, in the present case, it may be advisable to give estrogenic substance in the form of theelin, theelol, Amniotin or other product by mouth or hypodermically or both. The exact dose cannot be stated but one may begin by administering 50 or 100 rat units daily during the menstrual period or as long as the headaches last (larger doses are required by mouth). Preparations of anterior pituitary-like gonadotropic hormone such as Antuitrin S or Follutein may be tried if estrogenic substance fails. Recently some patients with headaches of the migraine type have been relieved by the hypodermic use of ergotamine tartrate (Gynergen). Some cases of headaches apparently not migraine have also been helped by this preparation; others do not respond to it. Ergotamine tartrate does not ordinarily prevent headaches, but it may produce fairly rapid relief from cephalalgia. Other patients with migraine and migraine-like headaches have been considerably relieved by chondroitin sulphuric acid. This drug is best taken in capsule form and about nine capsules of 0.6 Gm. each are taken daily.

DANGERS OF DICHLORBENZENE

To the Editor:—Having noted in Queries and Minor Notes in THE JOURNAL, Oct. 13, 1934, page 1174, a question as to the dangers of benzene dichloride, I thought it might be of interest to relate a personal experience. A patient of mine, a woman in her twenties, who was exceptionally strong, healthy and athletic, spent almost an entire day packing away winter clothing and furs with the crystals of Dichloricide. That night she slept in the same room as was the closet in which she had stored the clothes. The door did not close tightly, and hence the fumes from the Dichloricide freely entered the room. In the morning there was noted marked swelling of the hands, feet and ankles. The young woman did not feel ill but was aghast to find that she had gained 6 pounds since the previous morning. This great increase of weight was evidently due to a retention of fluids. The urine was quite normal. She played golf on that and the following days, and at the end of about three days the swelling had disappeared, and the weight returned to normal. There seems no reason to doubt that the retention of fluids was due to the inhalation of the Dichloricide fumes. It seems likely that this was due to some effect on the walls of the small blood vessels, causing an unusual transudation of serum into the tissues. There appeared in THE JOURNAL, Feb. 10, 1934, page 461, an editorial entitled "Benzene as a Cardiac and Vasomotor Poison" which may throw some light on this case. I should be glad if you would give me your opinion on this subject.

THOMAS A. CLAYTOR, M.D., Washington, D. C.

ANSWER.—We have been unable to find any record in the literature of poisoning from paradichlorbenzene, although one case was recently reported of intoxication from monochlorbenzene. As the introduction of chlorine into the benzene molecule is said not materially to modify the toxicity of the substance, it is conceivable that poisoning could arise from paradichlorbenzene under special conditions. As was pointed out in the query and minor note in question, the possibility of intoxication by this compound is ordinarily limited by the fact that it is a solid at ordinary temperatures; nevertheless the fumes must be active by reason of the fact that the vapors alone act as an insecticide. For this reason the edema reported by Dr. Claytor may well have been caused by this substance, though this is by no means certain.

RESIDUAL EFFECTS OF CARBON MONOXIDE POISONING

To the Editor:—I would appreciate some information with regard to the residual effects from carbon monoxide poisoning. Is it possible after an individual has apparently recovered from a single poisoning from this gas to be left with a damaged condition of the lungs and blood and to drag along for a couple of months showing very few symptoms? What is the usual length of time that it takes for the pneumonia that may result from such poisoning to manifest itself? Also what is the longest interval that may elapse between exposure and incidence of pneumonia? Is it necessary in order to have a condition of chronic carbon monoxide poisoning for one to come repeatedly in slight contact with the gas day after day, or can a condition of chronicity result from one severe exposure to the gas? Any references on acute and chronic carbon monoxide poisoning will be appreciated. Please omit name.

M.D., Louisiana.

ANSWER.—In the large majority of cases of carbon monoxide poisoning, if the patient does not die in the gas, consciousness returns in, at most, a few hours and recovery from the ill effects of the gassing is complete within a few days. It is only after an exposure of many hours to a sublethal concentration of carbon monoxide that injuries to the nervous system and mentality, and occasionally to other organs and functions, develop and persist throughout the remainder of life. If pneumonia does not develop within a week, its subsequent development cannot well be charged as due to asphyxia. Chronic carbon monoxide poisoning can occur only under conditions of frequent exposure, and not from one severe exposure, other than the residual effects referred to. Further information regarding acute poisoning is given by Yandell Henderson in an article entitled "The Dangers of Carbon Monoxide Poisoning and Measures to Lessen These Dangers," THE JOURNAL, Jan. 18, 1930, page 179, and "Resuscitation," THE JOURNAL, Sept. 8, 1934, page 750, and September 15, page 834. Information on the more obscure subject of chronic poisoning is given by Dr. Alice Hamilton in "Industrial Toxicology," New York, Harper and Brothers, 1934.

HEPATIC CIRRHOSIS

To the Editor:—Are injections of liver extract in any way beneficial in treating hepatic cirrhosis (atrophic or alcoholic)? I should also appreciate information as to any new remedy or surgical treatment that would help in such a case of cirrhosis.

GENEROSO LOMBARDI, M.D., Brooklyn.

ANSWER.—Injections of liver extract are of value when an anemia is present, possibly owing to the absence of the intrinsic substance in such a cirrhosis.

In some cases the ascites may be relieved and held in abeyance by medical treatment. The patient should receive daily doses of one of the acid base salts, as ammonium nitrate, 2 Gm., four times a day, and be given an injection of one of the mercurial diuretics every third day until the ascitic fluid has disappeared, when the mercurial diuretic may be discontinued but the acid base salts continued. At the first reappearance of the fluid, the mercurial diuretic should be resumed.

The Talma-Morrison operation has given the best results. The percentage of cures is not available in any large series of cases. The operation consists in drawing large masses of the omentum into pockets made between the peritoneum and the anterior abdominal wall. The omentum may be rubbed or abraded, but this is not considered essential. The diaphragmatic surface of the liver may be rubbed with gauze and the same action carried out on the under surface of the diaphragm, if the patient is in good condition after the omentum has been placed in the peritoneal pouches. However, in some cases the abrasion of the upper surface of the liver and the lower surface of the diaphragm has caused serious shock. About one patient out of six will be fairly well for a number of years.

EXTRASYSTOLES

To the Editor:—I am troubled much with extrasystoles. The condition is worse when I go to bed and often interferes with my falling asleep. Occasionally I am awakened with a severe attack, usually toward morning. I am also troubled with severe hyperacidity of a nervous character, as no evidence of ulcer has been found. The size of the heart is normal; compensation for my age (51) is good. A cardiogram shows nothing abnormal. What treatment would you suggest for the troublesome extrasystoles? Please omit name.

M.D., New York.

ANSWER.—Extrasystoles in the absence of any other evidence of heart disease are unimportant except as they may cause troublesome sensations. Sir James Mackenzie's advice was, first, reassurance about the significance of extrasystoles in such cases; second, the omission of any toxic or irritating factor such as tobacco, indigestion or fatigue; third, exercise in the open air, and, finally, if necessary, the use of some sedative, particularly bromides. Authoritative cardiovascular opinions at the present time agree with this old advice of Mackenzie's with the additional suggestion of trying quinidine sulphate from 0.13 to 0.2 Gm. (2 to 3 grains) three or four times a day, particularly at bedtime, when extrasystoles are more prone to occur or to be noticed.

Hence it is well to correct factors such as the overuse of tobacco, tea, coffee, heavy meals at night, long fatiguing hours, and lack of exercise. If these measures do not suffice, a trial of bromides is advisable, 0.5 Gm. (7½ grains) three or four times a day, or of quinidine sulphate in the dosage mentioned, or of the two together for a week or two or three at a time, as needed. If this additional measure does not suffice, the extrasystoles should be ignored so far as possible. One becomes accustomed to them in time and may not notice them at all eventually.

There is a relationship to hyperacidity in some patients. Digestive disturbances frequently act reflexly on the heart.

ABSORPTION BY RECTUM

To the Editor:—I am interested in the new theories as to absorption of dextrose saline, saline solution, coffee, and so on, when given by rectum. Could you send me literature concerning this or advise me where to find that information?

MALCOLM D. HARRISON, M.D., Washington, D. C.

ANSWER.—The following references might be of value to the inquirer:

Bross, W., and Kubikowski, P.: Hemodynamics as Test of Absorption of Alimentary Substances Introduced by Way of Rectum, *Polska gaz. lek.* **13**: 194 (March 11) 1934.

Collens, W. S., and Boas, L. C.: Absorption of Dextrose by Rectum, *Arch. Int. Med.* **52**: 317 (Aug.) 1933.

Clement, R.: Advantages of Rectal Administration of Cod Liver Oil, *Presse méd.* **41**: 1001 (June 21) 1933.

Ramond, F.; Guittonneau, G., Nicholas and Chevalier: Therapeutic Action of Wine Injections and Enemas, Progrès méd., Aug. 12, 1933, p. 1417.

Bauer, J., and Mongula, J.: Sugar Metabolism in Relation to Resorption of Sugar Administered by Rectum, *Klin. Wchnschr.* **11**: 1820 (Oct. 29) 1932.

Scott, E. L., and Sweighart, J. F. B.: Blood Sugar in Man Following Rectal Administration of Dextrose, *Arch. Int. Med.* **49**: 221 (Feb.) 1932.

Julesy, M., and Winkler, E.: Effect of Rectal Administration of Concentrated Dextrose Solution on Blood Sugar, *Ztschr. f. d. ges. exper. Med.* **80**: 823, 1932.

Trabucchi, E.: Rectal Injections of Hydrogen Sulphide in Treatment of Poisoning with Mercuric Chloride, *Boll. de soc. Ital. di. biol. sper.*, September 1931, p. 893.

Julliard, C.: Use of Hypertonic Saline Enema in Treatment of Preoperative Flatulence Before Reestablishment of Normal Intestinal Conditions, *Schweiz. med. Wchnschr.* **61**: 665 (July 11) 1931.

McNealy, R. W., and Willems, J. D.: Absorption of Dextrose from Colon: Effects of Chemical Excitants on Dextrose Enema, *Arch. Surg.* **22**: 649 (April) 1931.

NO RELATIONSHIP BETWEEN ALUMINUM IN DIET AND FURUNCULOSIS

To the Editor:—I am writing in regard to aluminum poisoning in relation to furunculosis. I have under my care at the present time a family of seven children and the father and mother with multiple furuncles. The history begins three years ago when they purchased a heavy aluminum cooking set. At this time the entire family had never had any skin eruption or furuncles. Six months after the aluminum set had been purchased, two of the pots began to pit on the bottom. Six months after the pitting was noted, the smallest child in the family, 7 years of age, began to have boils in the gluteal region. One by one the entire family has had furuncles in the gluteal region and neck. One boy, aged 18 years, was in the hospital with multiple furuncles on the lateral surface of his left leg from the knee to the ankle. The lesion did not penetrate beyond the fascia. The leg was treated with hot packs, and after draining two months and general supportive treatment the wound cleared up. The boy seemed to have no resistance to this low-grade staphylococcic infection. I might mention that the family lives in a large house and has a married son living in the same house, but cooking and eating separately. He and his wife and two children did not have furuncles, although they were constantly together, except for their meals. I should like to know whether there is any relationship between furunculosis and aluminum poisoning. Of course, it is realized that aluminum should not pit.

CARL B. CONE, M.D., Vancouver, Wash.

ANSWER.—So far as known, aluminum in the tissues exists only in minute quantities and has at the maximum amount no deleterious effect when the phosphorus content of the diet is normal (Schwartze, E. W.; Cox, G. J.; Unangst, R. B.; Murphy, F. J., and Wigman, Helen B.: The Extent of the Retention of Ingested Aluminum, THE JOURNAL, Nov. 25, 1933, p. 1722). The boils are due to some other factor common to the members of this family. It may be a fault in diet, poor choice of foods, bad cooking, contamination of food by some poison, the use of "patent medicines," or an infection to which the other family is not exposed.

ALLERGIC RHINORRHEA

To the Editor:—I have a patient, aged 14 years, who has suffered from asthma for many years. Skin tests have been positive for foods and many other substances, all of which have been eliminated and at present the chest shows no sign of asthma. The patient now sneezes a great deal alternately with periods of "stuffed nose." Examination of the nose shows enlargement of the left inferior turbinate. Do you feel that cauterization will relieve or cure the nasal condition? What possible ill effects can cauterization have on the original asthmatic condition? Please omit name.

M.D., New York.

ANSWER.—From the history as given, the attacks of sneezing and the periods of stuffed nose would lead one to make a diagnosis of vasomotor or allergic rhinorrhea. This diagnosis would be further substantiated if the mucosa of the nose has the characteristic waterlogged appearance seen in this condition, and if the secretions are thin and watery rather than thick and purulent.

Cauterization of a turbinate, such as described, will for varying periods and in a number of instances improve the airway. It frequently fails to do so. Cauterization in itself cannot cure the nasal condition, which rests, in all likelihood, on a sensitivity similar to the one that caused the asthma. It is hardly likely that the asthmatic condition will be made worse by the cauterization. In fact, from time to time, and for no apparent good reason, minor nasal interventions have been known to have a beneficial effect on asthma.

NEUROCIRCULATORY ASTHENIA

To the Editor:—A man, aged 42, has consulted me with complaints that are apparently due to "neurocirculatory asthenia" and nonspecific bronchitis. He attributes his subnormal health for more than fifteen years to being gassed with phosgene in the Argonne. He continued on active duty at the front until after the armistice a month later. Will you tell me what the probabilities are that a brief exposure to phosgene gas in October 1918 could have had such lasting effects? Particularly could it have caused the symptoms of cardiac neurosis? Please omit name.

M.D., Georgia.

ANSWER.—There is not even a possibility that the symptoms are due to any organic effects of the phosgene gas. The gas or other war experiences may have constituted sufficient psychic trauma. The possibility of some mild infection causing enough physical trauma must be considered but, with a history of fifteen years, is most improbable. But underlying all such cases is the "constitutional inferiority" of McFee Campbell, and in the more extreme cases little if any activating factor is needed.

The bronchitis should be closely investigated and the results checked by roentgen examination if this has not been done.

LABORATORY DIAGNOSIS OF GLYCOSURIA

To the Editor:—What is the most practical and efficient means of treating cases of diabetes mellitus with a high renal threshold while in the hospital, and later when discharged to the outpatient clinic? At the present time two ward patients have renal thresholds of 295 and 310 mg. per hundred cubic centimeters. The daily check with urinalysis is almost useless, for these tests are sugar free almost up to the onset of coma, and blood sugars every other day or so produce a secondary anemia as shown by a case treated here in the recent past. Please omit name and address.

M.D., Pennsylvania.

ANSWER.—When the renal threshold for sugar in diabetes mellitus is as high as described in these cases, the treatment must of course be controlled by reference to the blood sugar level rather than to the glycosuria. Aside from the presence of the ketone bodies in the urine, which represents too great a disturbance in the metabolism to be clinically useful as the sole guide to proper treatment, there is no other laboratory criterion of the diabetic state that does not involve blood sampling.

There seems to be no reason to believe that the secondary anemia observed in the patient from whom blood samples were taken every other day was anything more than a coincidence. However, this contingency may be entirely avoided by employing one of the several micromethods for blood sugar estimation that are available.

EFFECTS OF BENZINE ON PLEURA

To the Editor:—Will you please be kind enough to write me at your earliest convenience what action benzine would have on the pleura of the lungs, as to adhesions and the like.

PAUL W. JOHNSON, M.D., Winston-Salem, N. C.

ANSWER.—It is presumed that the question refers to the introduction of benzine directly into the pleura. If such is the query, then benzine probably as a local irritant would produce adhesions. Its use, however, for this purpose should not be encouraged, because benzine introduced in this way would be highly toxic and cause profound disturbance of the nervous system. It is also well known that benzine has a direct toxic effect on both lymphoid and myeloid tissues. There is, however, the question of the action of benzene by inhalation of the volatile substance. Such action might by irritation of the bronchi and alveoli cause cellular reactions that lead secondarily to pleural involvement. It is probable that such action might occur by benzene lowering the resistance of the tissues and causing secondary infection.

AUTONOMIC EPILEPSY (?)

To the Editor:—A white school girl, aged 14, has insomnia, also nervous twitching or tremor of the hands and feet, preceded the day before by attacks of vertigo. These attacks have come on every five to six weeks for the last five years. Birth was normal. She has had measles, mumps and whooping cough. The tonsils and adenoids were removed seven years ago. Her mental condition is good. Otherwise the history is negative. Menstruation is not established. She weighs 86 pounds (39 Kg.), her height is 59 inches (150 cm.) and she is poorly nourished. The head, eyes, ears, nose and throat are normal. There is no enlargement of the thyroid. The heart, lungs and abdomen are normal. The blood pressure is normal and the blood Wassermann and spinal fluid Wassermann reactions are negative. Hemoglobin is 75; red blood cells number 3,700,000; white blood cells, 7,400. The urine is normal. When seen during an attack of so-called nervousness the child would sit up in bed, fully conscious, with some tremors of the upper and lower extremities, the pulse rate rising to 130 per minute. This was of short duration—about five minutes. Please give diagnosis and suggest treatment. Please omit name.

M.D., Maine.

ANSWER.—The attacks described are not characteristic. Because of their recurrence in the same form they suggest some sort of periodic discharge corresponding in nature with migraine or with an autonomic variety of epilepsy. Careful neurologic examination, with special reference to the autonomic centers in the brain, is indicated. If this gives negative results, a search for sources of allergic reaction should be made. Until these studies are made, therapeutic efforts can be directed only toward an improvement in the general state of nutrition.

READING DIFFICULTY AND OPHTHALMIC EXAMINATIONS

To the Editor:—In the type of work in which I am engaged (child guidance clinic), I frequently have children referred to me who have some reading difficulty. The question of proper eye examination comes up, particularly as it is related to the etiologic factors in the reading difficulty. More than an ordinary eye examination is required. I would much appreciate it if you would outline what would be considered an adequate examination in view of the most recent developments, and the chief factors to be taken into consideration in remedial work. Please omit name.

M.D., Rhode Island.

ANSWER.—The first examination is of course a careful refraction under cycloplegia, preferably atropine. Possible heterotropia should then be ruled out, by the cover test. Heterophoria in a child is more difficult to determine until a mentality of at least 8 or 9 years has been reached. Binocular vision and fusion should be examined for with the amblyoscope and any of the standard stereoscopic charts. Predominance of one or the other eyes can be determined by the same methods. Mirror writing is of course self evident. The examination of the central visual field areas is possible in some children but only a few, particularly when searching for a paracentral scotoma and when determining the size of the blind spot. With the knowledge given by these suggested examinations, any possible ocular factor in reading difficulty can be eliminated.

ZINC PREPARATIONS IN GONORRHEA—TRICHLORO-ETHYLENE IN NEURALGIA

To the Editor:—1. Is zinc permanganate used in about the same percentage as zinc sulphate solution for urethral injection for gonorrhea? 2. Also, would you recommend the inhalation of trichloro-ethylene for facial neuralgia?

EDWIN O. SWANSON, M.D., St. Paul

ANSWER.—1. Zinc permanganate is a vigorous oxidizing agent. The strength of its solutions to be used for urethral injection must be patterned more after that of potassium permanganate than that of zinc. A strength of 1:2,000 might be considered average, with a range of from 1:1,000 to 1:4,000. Zinc permanganate is not official and it does not stand accepted by the Council on Pharmacy and Chemistry.

2. Trichloro-ethylene inhalation is worth trying in cases of facial neuralgia. It will give relief in some cases and fail completely in others.

Medical Examinations and Licensure

COMING EXAMINATIONS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written (Group B candidates).* The examination will be held in various cities throughout the country, April 29. *Oral (Group A and Group B candidates).* New York, June 10. Sec., Dr. C. Guy Lane, 416 Marlborough St., Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Final oral and clinical examination (Group A and Group B candidates).* Atlantic City, N. J., June 10-11. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: Philadelphia, June 8, and New York, June 10. *Applications must be filed before April 10.* Sec., Dr. William H. Wilder, 122 S. Michigan Blvd., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 8. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: Atlantic City, N. J., June 10, and St. Louis, Nov. 19. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Philadelphia, June 7-8. Sec., Dr. Walter Freeman, 1726 Eye St. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: San Francisco, May 10-12, and Atlantic City, N. J., June 8-10. Sec., Dr. Byrl R. Kirklin, Mayo Clinic, Rochester, Minn.

ARIZONA: Phoenix, April 2-3. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

COLORADO: Denver, April 3. Sec., Dr. Wm. Whitridge Williams, 422 State Office Bldg., Denver.

CONNECTICUT: *Endorsement.* Hartford, March 26. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden.

IDAHO: Boise, April 2. Commissioner of Law Enforcement, Hon. Emmitt Pfost, 203 State House, Boise.

ILLINOIS: Chicago, April 9-11. Superintendent of Registration, Department of Registration and Education, Mr. Eugene R. Schwartz, Springfield.

MINNESOTA: *Basic Science.* Minneapolis, April 2-3. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, April 16-18. Sec., Dr. E. J. Engberg, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 2. Sec., Dr. S. A. Cooney, 7 W. 6th Ave., Helena.

NATIONAL BOARD OF MEDICAL EXAMINERS: The examination will be held in all centers where there are Class A medical schools and five or more candidates desiring to take the examination, June 24-26. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

NEBRASKA: *Basic Science.* Omaha, May 7-8. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, May 6. Sec., Dr. Edward E. Hamer, Carson City.

NEW MEXICO: Santa Fe, April 8-9. Sec., Dr. P. G. Cornish Jr., 221 W. Central Ave., Albuquerque.

RHODE ISLAND: Providence, April 4-5. Dir., Department of Public Health, Dr. Edward A. McLaughlin, 319 State Office Building, Providence.

TENNESSEE: Memphis, March 25-26. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

California October Examination

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination held in Sacramento, Oct. 16-18, 1934. The examination covered 9 subjects and included 90 questions. An average of 75 per cent was required to pass. Forty-three candidates were examined, 38 of whom passed and 5 failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1934)	80.6, 87, 91.1
Stanford University School of Medicine		(1934)	86.1, 89.1
University of California Medical School		(1934)	84.1, 84.7, 84.9, 89.8
University of Southern California School of Medicine		(1934)	80.7
University of Colorado School of Medicine		(1927)	85.9
George Washington University School of Medicine		(1934)	82.9
Georgetown University School of Medicine		(1933)	77.3
Howard University College of Medicine		(1933)	85.3
Bennett College of Eclectic Medicine and Surgery, Chicago		(1915)	90
Chicago Medical School		(1927)	78.4
Loyola University School of Medicine		(1932)	87.9
Northwestern University Medical School		(1934)	84.2, 90.6
Rush Medical College		(1906)	78.4, (1933) 75.7
Univ. of Illinois College of Medicine		(1926)	82, (1934) 83.6, 87.7, 89
Johns Hopkins University School of Medicine		(1934)	83.6
Creighton University School of Medicine		(1934)	76.1, 83.6
Columbia University College of Physicians and Surgeons		(1934)	88.9
Syracuse University College of Medicine		(1933)	86.1
University of Cincinnati College of Medicine		(1934)	82
University of Oregon Medical School		(1933)	82.9, 85.3
Woman's Medical College of Pennsylvania		(1932)	81.4, (1933) 76.9
University of Wisconsin Medical School		(1932)	85.6
McGill University Faculty of Medicine		(1933)	81
Johann Wolfgang Goethe-Universität Medizinische Fakultät, Frankfurt-am-Main, Prussia, Germany		(1923)*	76.9

School	FAILED	Year Grad.	Per Cent
Creighton University School of Medicine		(1933)	73.4
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany		(1934)*	66.3
Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany		(1927)*	62
Universität Leipzig Medizinische Fakultät, Saxony, Germany		(1908)*	70
Regia Università degli Studi di Modena Facoltà di Medicina e Chirurgia		(1932)*	57.2

Twenty-two physicians were licensed by reciprocity and 2 physicians were licensed by endorsement from October 4 to November 22. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine		(1933, 2)	Colorado
Howard University College of Medicine		(1933)	Maryland
Rush Medical College		(1933)	Illinois
Indiana University School of Medicine		(1925, 2), (1930)	Indiana
State University of Iowa College of Medicine		(1932)	Iowa
Johns Hopkins University School of Medicine		(1933)	Maryland
Grand Rapids Medical College, Michigan		(1902)	Michigan
University of Michigan Medical School		(1918), (1927), (1929)	Michigan
University of Minnesota Medical School		(1930)	Minnesota
University Medical College of Kansas City, Missouri		(1899)	Kansas
University of Nebraska College of Medicine		(1925), (1932)	Kansas
Ohio State University College of Medicine		(1932)	Ohio
University of Oregon Medical School		(1932), (1933)	Oregon
Jefferson Medical College of Philadelphia		(1919)	Mississippi
University of Vermont College of Medicine		(1920)	Connecticut

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Rush Medical College		(1927)	N. B. M. Ex.
Harvard University Medical School		(1930)	N. B. M. Ex.

* Verification of graduation in process.

Michigan Endorsement Report

Dr. J. Earl McIntyre, secretary, Michigan State Board of Registration in Medicine, reports 51 physicians licensed by endorsement during 1934. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Arkansas School of Medicine		(1928)	Arkansas
College of Medical Evangelists		(1934)	California
University of Colorado School of Medicine		(1928)	Colorado
George Washington University School of Medicine		(1930)	Penna.
Emory University School of Medicine		(1932)	Georgia
Loyola University School of Medicine		(1928), (1933)	Illinois
Northwestern University Medical School		(1912), (1933, 2)	Illinois, (1929), (1933) Ohio, (1933) Colorado
Rush Medical College		(1925), (1929, 2), (1930)	Illinois
University of Illinois College of Medicine		(1933)	Illinois
Indiana University School of Medicine		(1928), (1932), (1933)	Indiana
State University of Iowa College of Medicine		(1932), (1933)	Iowa
University of Louisville Medical Department		(1909)	Indiana
University of Louisville School of Medicine		(1930), (1932), (1933)	Kentucky
Johns Hopkins University School of Medicine		(1924), (1932)	Maryland
St. Louis Medical College		(1881)	Missouri
St. Louis University School of Medicine		(1931, 2), (1933, 2)	Missouri
University of Nebraska College of Medicine		(1932, 3)	Nebraska
Cleveland College of Physicians and Surgeons		(1891)	Ohio
Ohio State University College of Medicine		(1931)	Ohio
Western Reserve University School of Medicine		(1927), (1932)	Ohio
University of Oklahoma School of Medicine		(1932)	Oklahoma
Temple University School of Medicine		(1930)	Penna.
University of Pennsylvania School of Medicine		(1913)	Penna.
Meharry Medical College		(1933)	Tennessee
Vanderbilt University School of Medicine		(1932)	Tennessee
Marquette University School of Medicine		(1933), (1934)	Wisconsin
University of Wisconsin Medical School		(1928)	Mass.
University of Manitoba Faculty of Medicine		(1930)	Illinois
University of Edinburgh Faculty of Medicine		(1929)	Georgia

Pennsylvania Reciprocity and Endorsement Report

Mr. W. M. Denison, director, Bureau of Professional Licensing, reports 8 physicians licensed by reciprocity and 4 physicians licensed by endorsement from Oct. 8 to Dec. 26, 1934. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Michigan Medical School		(1930)	Michigan
University of Minnesota Medical School		(1930)	Minnesota
St. Louis University School of Medicine		(1927), (1930), (1933)	Minnesota, Missouri
University of Missouri School of Medicine		(1904)	Missouri
Columbia University College of Physicians and Surgeons		(1931)	New York
Cornell University Medical College		(1932)	Ohio

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Maryland School of Medicine and College of Physicians and Surgeons		(1933)	N. B. M. Ex.
University of Oregon Medical School		(1929)	N. B. M. Ex.
University of Pennsylvania School of Medicine		(1931)	N. B. M. Ex.
Woman's Medical College of Pennsylvania		(1933)	N. B. M. Ex.

Book Notices

Synopsis of Pediatrics. By John Zahorsky, A.B., M.D., F.A.C.P., Professor of Pediatrics and Director of the Department of Pediatrics, St. Louis University Medical School. Assisted by T. S. Zahorsky, B.S., M.D., Assistant in Pediatrics, St. Louis University Medical School. Cloth. Price, $4. Pp. 359, with 83 illustrations. St. Louis: C. V. Mosby Company, 1934.

This is a compact, pocket sized volume, which has condensed modern pediatric knowledge into sixty chapters. It is suitable for the classroom teaching of the subject to the medical student and should be useful to the practitioner as a handy guide in general practice. The subject matter is carefully treated and, though condensed, the essential points in symptomatology, diagnosis and treatment are well covered. Theoretical discussion, when included, is brief and to the point, and diseases that concern more particularly other specialties have received short but adequate consideration. The volume well fills the gap that exists between the larger textbooks, with fuller theoretical discussions and references to the literature of pediatrics, and the small mimeographed manuals in use at some of the medical schools. It also allows the practitioner the chance to obtain a competent guide in a small volume. The senior author of this synopsis has long been a master in the teaching and practice of pediatrics. His experience has enabled him to condense the material so that there is no loss in value due to brevity, as is the case in many another synopsis. The book is well printed and the illustrations are excellent. It should find favor with medical students and practitioners alike because of its well arranged and condensed subject matter. It is probably within the range of the purse of the medical student, so that ownership should not be prohibitive.

Suprarrenales y metabolismo de los hidratos de carbono. Por Luis F. Leloir. Tesis de doctorado en medicina. Padrino de tesis, Prof. Dr. Bernardo A. Houssay. Universidad Nacional de Buenos Aires, Facultad de Ciencias Medicas. Paper. Pp. 188. Buenos Aires: Imp. A. Baiocco y Cía, 1934.

Numerous experiments have been performed to throw additional light on the relationship of the adrenal glands to carbohydrate metabolism. From the data obtained, these experiments indicate that excision of the adrenals causes a diminution in blood sugar. Extirpation of the adrenal medulla or denervation of both adrenals does not result in any appreciable alterations in blood sugar. Excision of the adrenal glands produces a great decrease in liver glycogen, occasionally causing it to disappear completely. Muscle glycogen is also lessened and the intravenous injection of dextrose results in still greater diminution in contradistinction to the increase that is seen in normal animals. Injection of adrenal cortex extract restores the blood sugar to normal. It is believed that there is an antagonistic action between epinephrine and insulin and that denervation and extirpation of the adrenal medulla increase the animal's sensitivity to insulin, but that complete excision of the adrenal causes a still greater sensitivity to insulin.

The Physical and Mental Growth of Prematurely Born Children. By Julius H. Hess, M.D., Professor of Pediatrics, College of Medicine, University of Illinois, Chicago, George J. Mohr, M.D., Director, Pittsburgh Child Guidance Center, and Phyllis F. Bartelme, Ph.D., Psychologist, Cook County Juvenile Court, Chicago. Cloth. Price, $5. Pp. 449, with 90 illustrations. Chicago: University of Chicago Press, 1934.

The authors are well known for their current contributions on the subject of prematurely born children. This book probably contains more original research and statistical data than any other book on the subject. The senior author is well known for his previous authoritative book on premature infants, published some years ago for the physician. In this book, however, are correlated physical and mental development, with the result that it is perhaps unique of its kind. The question of what type of physical and mental progress the prematurely born infant makes is admirably answered. Several chapters on related medical aspects of premature children are contributed by other well qualified authors. The organization of the book is excellent, considering the amount of data utilized. There are numerous valuable tables and graphs which enable the reader to crystallize the descriptive material. The value of the book will be readily apparent to those charged with the medical care of prematurely born children. It, however, will serve with almost equal value those interested in psychology and child welfare. The book is a distinct contribution to the literature on medical and social science and should be the property of every medical library.

"Ererbte Taubheit": Grundzüge zur Erkennung ererbter Hörstörungen, soweit sie das Gesetz zur Verhütung erbkranken Nachwuchses betreffen. Von Prof. Dr. M. Schwarz, Oberarzt der Universitäts Hals-, Nasen- und Ohrenklinik Tübingen. Paper. Price, 4 marks. Pp. 56, with 28 illustrations. Leipzig: Georg Thieme, 1935.

This monograph includes a discussion of the laws of heredity and the incidence of dominant and recessive factors under a variety of combinations as well as a study of the various types of deafness in relationship to heredity. The forms of deafness considered are recessive as well as sporadic deafmutism, hereditary-degenerative inner ear deafness, endemic or deafness of cretinism, otosclerosis, and deafness, complete or partial, the result of chronic inflammatory processes of the middle ear in which a lessened resistance of the mucosa is the recurring factor. Each of these types is discussed rather fully as to incidence, mode of hereditary transmission, presence of other physical characteristics, diagnosis, method of examination and sociological implications. In line with the policy of the German state concerning defectives, the author recommends sterilization in all but the strictly middle ear types of deafness.

The 1934 Year Book of Radiology. Diagnosis. Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University. Therapeutics. Edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York. Cloth. Price, $4.50. Pp. 512, with 454 illustrations. Chicago: Year Book Publishers, Inc., 1934.

As customary, this issue is divided into a diagnostic section and a section dealing with therapy. The literature has been well reviewed and condensed, with occasional footnotes expressing the author's point of view, which is valuable. Both authors apologize for the scarcity of original material, which is due to the economic condition. This attitude is a reflection of their modesty, because much of the material is quite valuable, as it represents variations in technic, amplification of many unusual conditions, and a reiteration of known experiences. Disease processes know no formulas, and it is just as important to become familiar with simulants, variants and heterotopic forms as to become acquainted with the classic forms and methods, which, after all, are infrequent. It can well be said that, should future editions be as informative as those of the past, a perpetual endorsement can be assured.

Kompendium der topischen Gehirn- und Rückenmarksdiagnostik: Kurzgefasste Anleitung zur klinischen Lokalisation der Erkrankungen und Verletzungen der Nervenzentren. Von Robert Bing, ordentlicher Professor an der Universität Basel. Ninth edition. Paper. Price, 9 marks. Pp. 227, with 127 illustrations. Berlin & Vienna: Urban & Schwarzenberg, 1934.

Twenty-five years has passed since Professor Bing published his first compend on diagnosis of brain and spinal cord diseases. In the present edition he has written a modern, excellent and detailed text despite the fact that the book is only a compend. Bing divides the subject matter into two parts: (*a*) the topical diagnosis of spinal cord disorders; (*b*) topical diagnosis of brain disorders. The topical diagnosis of spinal cord disorders takes up in detail the topographical anatomy of the spinal cord in regard to the diagnosis of lesions involving the various pathways, that is, motor, sensory, trophic, vasomotor and pilomotor, both as separate and combined lesions. It further considers the anatomic and physiologic foundations for localization of the level of any lesion, central, radicular or peripheral. The topical diagnosis of brain disorders deals with the basic fundamentals of structure and the localization of lesions of the brain stem, cerebellum, brain, basal ganglions and hypophysis. Encephalography and ventriculography are discussed in relation to their indications and interpretations. The book is clearly written and contains an unusual amount of current anatomic and physiologic thought. His method of presenting the material of neurologic diagnosis is practical and easy to assimilate. This compend contains all that is needed for the student to get a thorough understanding and rationalization in the interpretation of neurologic signs and symptoms. It may be highly recommended.

The Cyclopedia of Medicine. George Morris Piersol, B.S., M.D., Editor-in-Chief, and Edward L. Bortz, A.B., M.D., Assistant Editor. Chief Associate Editors: W. Wayne Babcock, A.M., M.D., Conrad Berens, M.D., P. Brooke Bland, M.D., Francis L. Lederer, B.S., M.D., and A. Graeme Mitchell, M.D. Volume XII: TEN-ZONA. Fabrikoid. Price, $120 per set of 12 volumes and index. Pp. 1004, with illustrations. Philadelphia: F. A. Davis Company, 1934.

This volume begins with the tendons, and after discussing such leading topics as tetanus, thermic injuries, the thorax, thrombosis, the thyroid and thymus, tobacco and the tongue, tremors and tuberculosis, it goes on to tumors, typhoid urinalysis, urology, urticaria, the uterus, the veins and the vitamins, the vulva and vagina, and those limited medical topics which come under x, y and z. It is well up to the standard maintained by the previous volumes. Such leading authors as J. D. Barney, Victor Bonney, Lawrason Brown, Leo Buerger, George Crile, Allen K. Krause, Matas, Musser, Pemberton and Webb are included among the contributors. The book is exceedingly well illustrated and is printed two columns to the page in easily readable type. Each topic is fully outlined and much extraneous matter has been eliminated. The work is thereby made most practical. It will appeal especially to the general practitioner who wants a ready reference work with emphasis on treatment.

Handbook of Filterable Viruses. By R. W. Fairbrother, M.D., M.R.C.P., Lecturer in Bacteriology and Assistant Director of the Public Health Laboratory, Manchester University. Cloth. Price, 7/6. Pp. 193. London: William Heinemann, Ltd., 1934.

The first half of this small volume consists of a summary of the nature, methods of study and classification of viruses, and the epidemiology and immunity of virus diseases. Current opinions are concisely expressed and controversial matters are reduced to a minimum. The author takes the view that viruses are biologic units. The second half of the book contains short descriptions of certain diseases of man and lower animals, grouped according to whether they are "accepted," "probable" or "possible" virus diseases. Experimental studies are summarized in each case. The author has condensed much information into a few pages and is to be commended for the result. The style is direct and the book is easily read. A list of references is given with each section; in some instances the choice of reference does not seem judicious. The experimental work in this field has proved exceptionally fruitful in recent years and a better acquaintance with the advances made is readily obtainable by the perusal of this handbook. For this reason it is useful to the acquiring student and inquiring physician.

Who Shall Survive? A New Approach to the Problem of Human Interrelations. By J. L. Moreno, M.D. Nervous and Mental Disease Monograph Series No. 58. Cloth. Price, $4. Pp. 437, with illustrations. Washington, D. C.: Nervous & Mental Disease Publishing Company, 1934.

This highly technical work is an attempt to analyze the emotional relationships of human beings in the business and the social world, based on the feelings of human beings toward one another. The method of study is unusual. On the basis of this type of study the author attempts to analyze such racial difficulties as have developed in Germany, and to outline a plan for new types of social organization. In the series of supplements the author provides a study of children's reactions to one another in schools and of workers' reactions to one another in shops.

L'hypertréphocytose: Cancérisation et cicatrisation. Par le Docteur Pierre Lemay, docteur de l'Université. Paper. Price, 20 francs. Pp. 169. Paris: Librairie E. Le François, 1934.

This work deals with the author's hypothesis based on the experimental research of Carrel concerning trephones. The author's conclusions, which he admits are only theoretical, do not agree with conclusions drawn by Carrel. According to the author there are two antagonistic substances that control the life and proliferations of the cell: the trephones, which stimulate, and antagonistic substances, which inhibit. In young individuals the trephones predominate; in older individuals the antagonistic substances predominate. A disturbance in the balance of these substances, which results in overactivity of the trephones, causes (1) growth and general development of the embryo, (2) cicatrization and (3) cancerization. When the antagonistic substances predominate, the result is aging, death, and cessation of cicatrization. According to this conception, general growth is looked on as hypertrephocytosis, aging as hypotrephocytosis, and cicatrization as localized momentary hypertrephocytosis. Cancerization is localized and uncontrolled hypertrephocytosis. Since in older persons the balance is in favor of inhibitory substances, tumor growth is slower than in young persons. The author believes that the action of the trephones is related to the activity of ferments. In support of his hypothesis he quotes a collection of his publications on this subject for the last ten years.

How to Practice Medicine. By Henry W. Kemp, M.D. Cloth. Price, $2.50. Pp. 156. New York: Paul B. Hoeber, Inc., 1935.

In this book a practitioner advises young men how to set themselves up in practice. He also offers practical information concerning their relationships to other practitioners, the etiquette of making calls, and their relationships to nurses, women and children. He discusses the care of the child, and obstetrics in general practice, and concludes with many simple hints on various phases of medical work. There is some advice for the aged, and some prescriptions are presented which the author has apparently found useful in his work. Unfortunately, in these prescriptions he violates many of the best rules regarding prescription writing and uses for his vehicles some compounds that are essentially "shotgun" prescriptions in themselves. The exceedingly young man who is naive may find a few hints in this work that will be most valuable to him in his beginning of medical practice.

The Constitution and Its Reaction in Health. By T. E. Hammond, F.R.C.S., Assistant Surgeon, The Royal Infirmary, Cardiff. Cloth. Price, 7/6. Pp. 160. London: H. K. Lewis & Company, Ltd., 1934.

The rather difficult title of this book does not express its contents. The book is essentially a textbook of personal hygiene. The author begins with six chapters on the constitution of man and his reactions to the seasons, to the weather and to nature generally. He classifies human bodies as hyposthenic and hypersthenic from the constitutional point of view. He then discusses all the common aspects of living in relationship to the human body, illustrating his discussions with brief notes of interesting cases. While much that is presented in this book is useful, it will strike the average American medical reader as most elementary and hardly on a par with some works available in this country.

The Advance of Science. Edited by Watson Davis, Director, Science Service, Washington, D. C. Cloth. Price, $3.50. Pp. 400, with illustrations. Garden City, N. Y.: Doubleday, Doran & Company, Inc., 1934.

This volume attempts to summarize knowledge in many scientific fields and to present it in a manner understandable to the average well educated reader. The considerations include not only chemistry and physics but also geography, physiology, pathology, biology, eugenics and many other related topics. For the reader who wants a cursory survey of experimentation and of the newer discoveries, the volume should prove attractive. For the special reader it is far too diffuse to be significant. It is a most useful text, however, in indicating the manner in which Science Service makes modern science understandable.

Chemioterapia del cancro. Dal Prof. G. Fichera. Paper. Price, 25 lire. Pp. 213, with 20 illustrations. Milan: Ulrico Hoepli, 1935.

This is the author's report on the chemotherapy of cancer to the international congress in Madrid in 1933. The report gives a long review of the literature on the subject, with an extensive bibliography. An index would have been helpful. Many kinds of treatment have been tried without success and no form of chemotherapy of cancer is beyond the experimental stage.

Manual of Clinical Laboratory Methods. By Pauline S. Dimmitt, Ph.G., Medical Technologist for the Stout Clinic, Sherman, Texas. Cloth. Price, $2. Pp. 156, with 36 illustrations. Philadelphia: F. A. Davis Company, 1934.

This small volume concerns itself primarily with the details of clinical laboratory procedures. The data are presented in almost outline form and cover the usual list of subjects found in books of clinical laboratory methods. Outside of its simplicity, the book has little to recommend it to the practicing physician. For the student it lacks the detail necessary for the development of a rational understanding of laboratory methods or their clinical application.

Medicolegal

Contract to Perform Vasectomy Not Against Public Policy.—The plaintiff's wife had experienced great difficulty with the birth of her first child and had been advised that it would be dangerous to her life to bear another. The defendant-physician was consulted by the plaintiff and advised that a vasectomy be performed on the plaintiff. The operation was performed, and, it was alleged, the defendant-physician pronounced it successful and guaranteed the sterility of the husband. Notwithstanding the operation, however, the plaintiff's wife again became pregnant. The wife survived the birth of the baby but the plaintiff sued the defendant-physician to recover damages for the great anxiety the pregnancy had caused him and for the expenses incurred in connection therewith. The trial court sustained a demurrer to the complaint on the ground that the contract and performance of the operation were against public policy and that the law would leave the parties where they placed themselves. The plaintiff thereupon appealed to the Supreme Court of Minnesota.

The plaintiff in this case based his cause of action solely on the failure of the operation to fulfil the defendant's alleged promise. The complaint did not charge lack of skill, malpractice, or negligence in any respect in the performance of the operation. The first question presented, said the Supreme Court of Minnesota, is whether a contract to perform such an operation under the circumstances here presented is against public policy and for that reason void. No authorities bearing directly on this question were cited by either party to the suit and the court itself could find none. There is in Minnesota, said the court, no statutory prohibition against sterilization. The plaintiff was married and presumably would remain married to his present wife, who had been competently advised of the danger of further pregnancy. The operation of sterilization on a man is a simple one, said the court, accompanied by very slight hazards, whereas that on a woman is more serious and requires a greater degree of skill on the part of the physician. It entails hospitalization. It is frequently performed on women who habitually miscarry or abort. So far as progeny is concerned, the results to this married couple would be the same were effective sterilization performed on either. Therefore, in the opinion of the court, it was entirely justifiable for them to take the simpler and less dangerous alternative and have the husband sterilized. Such an operation does not impair, but frequently improves, the health and vigor of the patient. Except for his inability to beget children, he is in every respect as capable physically and mentally as before. It does not render the patient impotent or unable "to fight for the king," as was the case in mayhem or maiming. The court concluded that under the circumstances the contract was not void as against public policy nor was the performance of the operation illegal on that account.

The plaintiff contended, however, that his complaint was grounded on deceit, and relied on the case of *Hedin v. Minneapolis M. & S. Institute*, 62 Minn. 146, 64 N. W. 158, 35 L. R. A. 417, 54 Am. St. Rep. 628. But, said the Supreme Court, there was no allegation of fraudulent intent on the defendant's part or any of the elements of deceit. In such an action the plaintiff must allege and prove, not only that the representation was false, but also that it was made with fraudulent intent. In the Hedin case there was abundant evidence to support the jury in finding that the defendant-physician must have known that his promise of cure could not be performed. The plaintiff in the present action did not seek to recover for breach of contract; he alleged no malpractice. He admitted that the operation he contracted for was performed. It is a matter of common knowledge that such an operation properly done in due course effects sterilization. It is in common use in states which authorize sterilization of defectives. Any competent physician or surgeon must necessarily have given the plaintiff advice to that effect. The purpose of the operation was to save the wife from the hazards to her life which were incident to childbirth. It was not the alleged purpose to save the expense incident to pregnancy and delivery. The wife survived. Instead of losing his wife, the plaintiff has been blessed with the fatherhood of another child. The expenses alleged are incident to the bearing of a child, and their avoidance is remote from the avowed purpose of the operation. As well might the plaintiff charge the defendant with the cost of education of the child. Although the validity of the contract was upheld, the judgment sustaining defendant's demurrer was affirmed. The action of the trial court, sustaining a demurrer to the complaint, was affirmed.—*Christiansen v. Thornby (Minn.), 255 N. W. 620.*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Mobile, April 16-18. Dr. D. L. Cannon, 519 Dexter Avenue, Montgomery, Secretary.

American Association of Anatomists, St. Louis, April 18-20. Dr. George W. Corner, University of Rochester School of Medicine, Rochester, N. Y., Secretary.

American Association of Pathologists and Bacteriologists, New York, April 18-19. Dr. Howard T. Karsner, 2085 Adelbert Road, Cleveland, Secretary.

American Association of the History of Medicine, Atlantic City, May 6. Dr. Edward J. G. Beardsley, 1919 Spruce Street, Philadelphia, Secretary.

American Association on Mental Deficiency, Chicago, April 25-27. Dr. Groves B. Smith, Beverly Farms, Godfrey, Ill., Secretary.

American College of Physicians, Philadelphia, April 29-May 3. Mr. E. R. Loveland, 133 South 36th Street, Philadelphia, Executive Secretary.

American Dermatological Association, White Sulphur Springs, W. Va., May 2-4. Dr. William H. Guy, 500 Penn Avenue, Pittsburgh, Secretary.

American Pediatric Society, Cleveland, May 2-4. Dr. Hugh McCulloch, 325 North Euclid Avenue, St. Louis, Secretary.

American Physiological Society, Detroit, April 10-13. Dr. Frank C. Mann, Mayo Clinic, Rochester, Minn., Secretary.

American Psychiatric Association, Washington, D. C., May 13-17. Dr. William C. Sandy, State Education Building, Harrisburg, Pa., Secretary.

American Society for Clinical Investigation, Atlantic City, May 8. Dr. H. L. Blumgart, 330 Brookline Avenue, Boston, Secretary.

American Society for Experimental Pathology, Detroit, April 10-13. Dr. Shields Warren, 195 Pilgrim Road, Boston, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Detroit, April 10-13. Dr. E. M. K. Geiling, 710 N. Washington Street, Baltimore, Secretary.

American Society of Biological Chemistry, Detroit, April 10-13. Dr. H. A. Mattill, State University of Iowa, Iowa City, Secretary.

Arizona State Medical Association, Phoenix, April 25-27. Dr. D. F. Harbridge, 15 East Monroe Street, Phoenix, Secretary.

Arkansas Medical Society, Fort Smith, April 15-17. Dr. W. R. Brooksher, 602 Garrison Avenue, Fort Smith, Secretary.

Association of American Physicians, Atlantic City, May 7-8. Dr. James H. Means, Massachusetts General Hospital, Boston, Secretary.

California Medical Association, Yosemite, May 13-16. Dr. F. C. Warnshuis, 450 Sutter Street, San Francisco, Secretary.

District of Columbia, Medical Society of the, Washington, May 1. Dr. C. B. Conklin, 1718 M Street N.W., Washington, Secretary.

Federation of American Societies for Experimental Biology, Detroit, April 10-13. Dr. H. A. Mattill, State University of Iowa, Iowa City, Secretary.

Florida Medical Association, Ocala, May 13-15. Dr. Shaler Richardson, 111 West Adams Street, Jacksonville, Secretary.

Georgia, Medical Association of, Atlanta, May 7-10. Dr. Allen H. Bunce, 139 Forrest Avenue N.E., Atlanta, Secretary.

Iowa State Medical Society, Davenport, May 8-10. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.

Kansas Medical Society, Salina, May 8-10. Mr. Clarence Munns, Stormont Building, Topeka, Executive Secretary.

Louisiana State Medical Society, New Orleans, April 29-May 1. Dr. P. T. Talbot, 1430 Tulane Avenue, New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, April 23-24. Dr. Walter Dent Wise, 1211 Cathedral Street, Baltimore, Secretary.

Mississippi State Medical Association, Biloxi, May 14-16. Dr. T. M. Dye, McWilliams Building, Clarksdale, Secretary.

Missouri State Medical Association, Excelsior Springs, May 6-9. Dr. E. J. Goodwin, 634 North Grand Boulevard, St. Louis, Secretary.

Nebraska State Medical Association, Omaha, May 14-16. Dr. R. B. Adams, Center-McKinley Building, Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 7-8. Dr. Carleton R. Metcalf, 5 South State Street, Concord, Secretary.

New Jersey, Medical Society of, Atlantic City, April 30-May 2. Dr. J. B. Morrison, 66 Milford Avenue, Newark, Secretary.

New York, Medical Society of the State of, Albany, May 13-15. Dr. Daniel S. Dougherty, 2 East 103d Street, New York, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, May 6-8. Dr. L. B. McBrayer, Southern Pines, Secretary.

Oklahoma State Medical Association, Oklahoma City, May 13-15. Dr. L. S. Willour, 203 Ainsworth Building, McAlester, Secretary.

South Carolina Medical Association, Florence, April 23-25. Dr. E. A. Hines, Seneca, Secretary.

South Dakota State Medical Association, Pierre, May 13-15. Dr. John F. D. Cook, Langford, Secretary.

Tennessee State Medical Association, Nashville, April 9-11. Dr. H. H. Shoulders, 706 Church Street, Nashville, Secretary.

Texas, State Medical Association of, Dallas, May 13-16. Dr. Holman Taylor, 208 Medical Arts Building, Fort Worth, Secretary.

West Virginia State Medical Association, Wheeling, May 6-8. Mr. Joe W. Savage, Public Library Building, Charleston, Executive Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Periodicals are available from 1925 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

189: 157-304 (Feb.) 1935

Changing Cause of Death in Diabetes Mellitus. J. M. Flynn, Boston. —p. 157.
Studies in Diabetes Mellitus: III. Interpretation of Variations in Diabetes Incidence. E. P. Joslin, Boston; L. I. Dublin and H. H. Marks, New York.—p. 163.
Action of Thevetin, Cardiac Glucoside and Its Clinical Application. H. L. Arnold, Honolulu, T. H.; W. S. Middleton, Madison, Wis., and K. K. Chen, Indianapolis.—p. 193.
Quinidine and Strychnine in Treatment of Premature Contractions. J. B. Carter and E. F. Traut, Chicago.—p. 206.
*Cardiovascular Response to Subcutaneous Injection of Epinephrine and Pituitrin in Essential Hypertension. A. H. Elliot and F. R. Nuzum, Santa Barbara, Calif.—p. 215.
Malignant Nephrosclerosis (Malignant Hypertension). H. E. MacMahon and J. H. Pratt, Boston.—p. 221.
*Paradoxical Embolism. F. J. Hirschboeck, Duluth, Minn.—p. 236.
Metastatic Melanocarcinoma with Apparent Recovery. J. J. Eller and I. L. Schonberg, New York.—p. 240.
Multiglandular Syndromes Resembling Simmonds' Disease: Case Report. A. Weinstein, Nashville, Tenn.—p. 245.
Endogenous Origin of Early Pulmonary Tuberculosis: Anatomic View of Its Clinical Diagnosis. W. Pagel, Cambridge, England.—p. 253.
Is There a "Moral Center" in the Brain? N. S. Yawger, Philadelphia. —p. 265.
Recurrence of Facial Paralysis. H. R. Merwarth, Brooklyn.—p. 270.
*Pathologic Physiology of Neuroglandular System. G. Crile, Cleveland. —p. 276.

Cardiovascular Response to Injection of Epinephrine and Solution of Pituitary.—Elliot and Nuzum measured the blood pressure and pulse rate at intervals of five minutes over a period of one hour in thirty-two patients having essential hypertension, who had received a subcutaneous injection of 1 mg. of epinephrine. The average systolic pressure fell slightly over a period of thirty-five minutes and then returned to the preinjection level; the average diastolic pressure fell to a maximal low point at forty-five minutes and remained near that level throughout the remainder of the period. The average pulse pressure decreased. The average pulse rate rose. A degree of parallelism existed between changes in the systolic pressure and in the pulse rate of these patients, such that a rise in pressure was usually accompanied by a rise in pulse rate, and a fall in systolic pressure by either a lowered or an unchanged pulse. Elevation of systolic pressure may be primarily the result of cardiac stimulation by epinephrine, whereas the fall in diastolic pressure is attributable to arteriolar dilatation. In forty hypertensive patients studied in a similar manner after receiving a subcutaneous injection of solution of pituitary, a slight rise in the average diastolic pressure and an equally slight fall in the average systolic pressure were observed after twenty minutes. The average pulse rate was unchanged. In the same patient, an unusual response to the injection of solution of pituitary was not necessarily accompanied by a vigorous response to epinephrine. No constant or frequent deviation from the reported normal cardiovascular response to the subcutaneous injection of epinephrine and solution of pituitary could be demonstrated in this series of patients having essential hypertension.

Paradoxical Embolism.—Hirschboeck states that about 50 per cent of the instances of paradoxical embolism are associated with antecedent pulmonary embolism. A study of the intra-auricular blood pressure establishes the pressure as somewhat higher in the left auricle than in the right, assuring competence as far as any circulation of blood from the right auricle to the left auricle is concerned in a state of health. An anatomic patency is therefore associated with a physiologic competence. Any disturbance in the pressure relationship may favor the development of paradoxical emboli when thrombosis in the venous circulation is present. Haggart and Walker showed experimentally that a sudden occlusion of the left pulmonary artery caused an immediate rise in the pulmonary pressure of about 29 per cent, whereas with total pulmonary occlusion the pressure increased rapidly from 120 to 257 per cent, with an immediate fall in the systemic arterial pressure. A patent foramen ovale is the most common of all fetal relics. The literature generally recognizes this in all necropsies as between 30 and 35 per cent. Diagnostically, paradoxical embolism may be assumed as occurring in life if the patient is the subject of venous thrombosis, develops an embolus in the systemic circulation and, after a careful search, has no other apparent causes for arterial embolism. If pulmonary infarction precedes the embolic accident, the diagnosis is more certain. The author reports a case that illustrates the sequence of paradoxical emboli in the systemic circulation subsequent to venous thrombosis and in association with antecedent pulmonary embolism. It represents one of the rare instances in which an embolus is found "in transit" through the patent foramen ovale at the time of death.

Pathologic Physiology of Neuroglandular System.—Crile emphasizes that the brain and the sympathetic nervous system and the glands are indissolubly linked together in function; that the one component of the neuroglandular system that can be normally and pathologically conditioned is nerve tissue—that is, the brain and sympathetic nervous system; that the glands cannot be so conditioned; that the brain and the sympathetic system can be conditioned only with the collaboration of certain hormones, and that in the case of civilized man the rise especially of the thyroid has so facilitated the conditioning of the brain that man owes his distinctions and his diseases to this unique collaboration. In support of this conception, the author offers the clinical results of the application of this principle in 350 cases of hyperkinetic diseases improved by dekineticizing procedures.

Annals of Internal Medicine, Lancaster, Pa.

8: 777-892 (Jan.) 1935

Heart Block Due to Calcareous Lesions of the Bundle of His: Review and Report of Case with Detailed Histopathologic Study. W. M. Yater and V. H. Cornell, Washington, D. C.—p. 777.
Quantitative Studies on Increased Potency of Liver Extract by Incubation with Normal Human Gastric Juice. P. J. Fouts, O. M. Helmer and L. G. Zerfas, Indianapolis.—p. 790.
Correlation of Mineral Metabolism and Vegetative Nervous System in Thyroid Disease. J. Klein, Chicago.—p. 798.
Diseases of Nervous System Producing Dysfunction of Other Organs and Dysfunction of Other Organs Producing or Simulating Diseases of Nervous System. L. J. Pollock, Chicago.—p. 805.
*Macrocytic Anemia in Banti's Disease. D. O. Wright, New Orleans. —p. 814.
Alkalosis: Clinical Problem. C. T. Way and E. Muntwyler, Cleveland. —p. 818.
*Observations of Remissions in Hyperthyroidism Induced by Pregnancy Urine Extract. P. Starr and Helen Patton, Chicago.—p. 825.
Incidence of Streptococcic Infection in Cardiovascuiar Sclerosis. N. W. Jones and A. L. Rogers, Portland, Ore.—p. 834.
Explanation of Mechanism of Infantile Paralysis Production in Human Being. J. A. Toomey, Cleveland.—p. 854.
*Gastric Digestion: Simple Visual Test and In Vitro Studies. M. B. Levin and S. Raffel, Baltimore.—p. 865.

Macrocytic Anemia in Banti's Disease.—Wright reports a case of Banti's disease in which the blood count showed a definite change from a hypochromic microcytic type of anemia to a macrocytic type closely resembling pernicious anemia in the stage of remission. He studied a series of cases diagnosed as Banti's disease to show that a color index of more than 1 is much more frequent and the mean color index higher in the groups with evidence of portal cirrhosis than in those without this complication. It is a well substantiated fact that a macrocytic type of anemia frequently occurs in portal cirrhosis. From his case report and from the study of the cases of Banti's disease it is obvious to the author that a macrocytic (pernicioid) type of blood picture will appear when portal cirrhosis develops. Therefore the concept that Banti's disease is always accompanied by a microcytic type of anemia is erroneous.

Remissions in Hyperthyroidism Induced by Pregnancy Urine Extract.—Starr and Patton treated thirteen cases of hyperthyroidism with pregnancy urine extract and theelin. The

usual course of treatment lasted for four or five months. Remission of hyperthyroidism has occurred coincidental with the treatment in seven cases. The six failures seem to illustrate that the induction of remission by pregnancy urine extract is dependent on normal ovarian function. At the present time no physiologic proof that the remission occurring in these cases may be attributed to the pregnancy urine extract and theelin treatment can be given, because the mechanism of such an action is unknown. Nevertheless, remissions have occurred abruptly in the healthiest adolescent girl, and more gradually in adult women. In two cases the return of menstruation, which had ceased during pregnancy urine extract treatment, was coincident with remission, as evidenced by a gain of weight, previously stationary, and a reduction of the metabolic rate to or nearly to the normal zone.

Gastric Digestion.—Levin and Raffel found a microscopic method of estimation of gastric digestion based on the demonstrated ability of the gastric secretions to digest striae, connective tissue and nuclei to furnish a satisfactory index of gastric function (digestion). The mixture of secretions derived from the duodenum when combined with pepsin hydrochloric acid promotes the rapidity of digestion to a marked degree. Such increased activity occurs if the components are allowed to act on the test material at an appropriately low p_H. Under these conditions, neutralization of the acid after a short period inhibits the progress of the digestion only to some degree. When neutralization of the mixture is effected before it has come into contact with the test material, however, no digestive activity is manifested. On the basis of these observations, it is suggested that large doses of alkali be administered both before and after meals in cases of duodenal ulcer. Simultaneous experiments on the comparative digestibilities in vivo and in vitro of various animal proteins in the form of representative meats have indicated that a dried beef-liver preparation is of value in cases in which such proteins are desired but cannot be conveniently taken in the usual manner.

Annals of Surgery, Philadelphia

101: 1-658 (Jan.) 1935. Partial Index

Surgical Management of Brain Abscess. A. W. Adson and W. M. Craig, Rochester, Minn.—p. 7.
Cerebral Osteochondroma of Dural Origin. B. J. Alpers, Philadelphia. —p. 27.
Deafness as Psychologic Entity. G. Berry, Worcester, Mass.—p. 38.
Treatment of Acute and Chronic Cases of Cerebral Trauma, by Methods of Dehydration. T. Fay, Philadelphia.—p. 76.
*Intracranial Operations in Sitting Position. W. J. Gardner, Cleveland. —p. 138.
Tumors Arising from Sensory Root of Trigeminal Nerve in Posterior Fossa: Perineurial Fibroblastoma. M. A. Glaser, Los Angeles. —p. 146.
Brain Lesions and Duodenal Ulcer: Report of Two Cases. F. C. Grant, Philadelphia.—p. 156.
*Meningioma as Cause of Epilepsy. R. A. Groff, Philadelphia.—p. 167.
Deformation of Sella Turcica by Tumors in Pituitary Fossa. K. Kornblum and L. H. Osmond, Philadelphia.—p. 201.
Treatment of Causalgia by Thoracic Sympathetic Ganglionectomy. S. T. Kwan, Peiping, China.—p. 222.
Roentgen Diagnostic Significance of Erosion of Optic Canals in Study of Intracranial Tumors. H. K. Pancoast, Philadelphia.—p. 246.
Glossopharyngeal Neuralgia. M. M. Peet, Ann Arbor, Mich.—p. 256.
Dilatations of Cavum Septi Pellucidi and Cavum Vergae. E. P. Pendergrass and P. J. Hodes, Philadelphia.—p. 269.
Bilateral Paralysis of Facial and Abducent Nerves as Remote Effect of Tumor of Brain. W. G. Spiller, Philadelphia.—p. 329.
Decerebrate Rigidity in Children. E. S. Thorpe Jr., Philadelphia. —p. 338.
Benign Cysts of Cerebellum: Report of Two Cases. D. O. Vasiliu, Budapest, Hungary.—p. 347.
Aphasia in Brain Tumors. T. H. Weisenberg, Philadelphia.—p. 373.
Pathology of Acute Purulent Meningitis. N. W. Winkelman, Philadelphia, and J. L. Eckel, Buffalo.—p. 383.
Observations on Total Pulmonary Lobectomy and Pneumonectomy. J. Alexander, Ann Arbor, Mich.—p. 393.
Affections of Sphenopalatine Ganglion. E. H. Campbell, Philadelphia. —p. 429.
Nonsurgical Causes of Acute Abdominal Pain. B. I. Comroe, Philadelphia.—p. 438.
Push-Back Operation in Cleft Palate Surgery. G. M. Dorrance, Philadelphia.—p. 445.
Pilonidal Cysts: Treatment of Excision and Primary Suture in Ambulatory Patients. L. K. Ferguson, Philadelphia.—p. 469.
Cardiac Improvement Following Gallbladder Surgery: Electrocardiographic Evidence in Cases with Associated Myocardial Disease. T. Fitz-Hugh Jr. and C. C. Wolferth, Philadelphia.—p. 478.
*Effect of Superior Laryngeal Nerves on Tracheal Mucus: Experimental Study on Relationship. J. Johnson, Philadelphia.—p. 494.
Action of Glucose on Emptying of Stomach: Effect of Varying Concentrations in Both Normal Stomachs and After Various Gastric Operations. C. G. Johnston and I. S. Ravdin, Philadelphia.—p. 500.
The Gastric Ulcer-Cancer Problem. L. H. Landon, Pittsburgh.—p. 536.
*Use of Peritoneum in Repair of Inguinal Hernia. J. W. Levering, Philadelphia.—p. 550.
*Selective Thoracoplasty in Treatment of Pulmonary Tuberculosis. R. H. Overholt, Boston.—p. 576.
Obscure Pseudomembranous Trigonitis: Trigonitis Areata Alba. P. S. Pelouze, Philadelphia.—p. 594.
Primary Carcinoma of Liver with Spontaneous Rupture and Lethal Hemorrhage. T. G. Schnabel, Philadelphia.—p. 613.
Acute Empyema in Children: Report of Three Hundred and Ten Cases. C. R. Steinke, Akron, Ohio.—p. 617.
Complicated Dislocations. T. T. Thomas, Philadelphia.—p. 633.
Essential Hematuria: Clinical and Pathologic Study. D. L. Wilbur and J. T. Priestley, Rochester, Minn.—p. 647.

Intracranial Operations in Sitting Position.—Gardner recommends the sitting position of the patient combined with tribrom-ethanol anesthesia for operations on the cerebellum. This position results in (1) a diminution in bleeding, (2) a lowering of intracranial pressure, (3) a lessened tendency to immediate cerebral edema and (4) an improved respiratory exchange, and it also facilitates access to the patient, particularly by the anesthetist. This position is not recommended for operations on tumors about the sella turcica or on the inferior surfaces of the cerebral hemispheres. In other cerebral tumors the position is recommended with reservation, because of the tendency for an occasional patient to go into prompt and profound shock. The position has distinct advantages in cervical and upper dorsal laminectomy and in excision of the cervicodorsal sympathetic ganglions by the Adson approach. It does not predispose to postoperative hemorrhage.

Meningioma as Cause of Epilepsy.—In reviewing 291 cases of meningioma, Groff observed that the incidence of epilepsy in this series was 30.9 per cent, or ninety cases. In these ninety cases there were eighteen of severe, seven of mild and sixty-five of jacksonian seizures. The latter group was divided into thirty-six cases of a motor type of attack, twenty-two of a sensory motor spell and seven of a pure sensory seizure. Aside from these ninety cases there were twelve of uncinate fits. In fourteen of the eighteen cases of generalized convulsions the lesions were in the frontal lobe or the temporal lobe or arising from the sphenoid ridge. In fifty-four of the sixty-five cases of jacksonian epilepsy the tumors involved the frontal and parietal lobes. Ten of the twelve cases of uncinate fits presented tumors in close relationship to the uncinate gyrus. The incidence of epileptic seizure was greatest in tumors of the frontal, parietal and temporal lobe. There were 116 patients with tumors in this region, and eighty had convulsions. All except sixteen of these had focal attacks. In the twenty-one cases of tumor located in the posterior fossa, not one was complicated by convulsive seizures. Sixty-six patients had preoperative convulsions. Twenty-four were relieved after the tumor was removed in an average follow-up period of four years. Thirteen of the 201 patients without convulsions developed seizures after operation. Eight of these had jacksonian seizures, while the remaining five had severe attacks.

Effect of Superior Laryngeal Nerves on Tracheal Mucus.—It is apparent to Johnson that: 1. Stimulation of the peripheral ends of the recurrent and of the superior laryngeal nerves will cause a secretion of tracheal mucus. 2. A more abundant secretion is produced by pilocarpine. 3. Stimulation of the central end of the vagus or of the superior laryngeal nerves will cause a reflex secretion of mucus. 4. Direct stimulation of the tracheal mucosa will cause a secretion of mucus partially by direct irritation of the mucous glands and partially by stimulation of the mucous glands through a reflex arc. 5. These secretory mechanisms may be interrupted by atropine, except that of direct irritation of the mucous glands. 6. The demonstration of these facts together with the clinical observation presents fairly good presumptive evidence that there is a definite relationship between injury to the superior laryngeal nerves during thyroidectomy and the formation of postoperative tracheal mucus.

Peritoneum in Repair of Inguinal Hernia.—Levering studied the tensile strength of various fasciae in dogs and compared these observations with similar studies made on the tensile strength of the peritoneum of the same animals. It seemed possible that some structure readily available in certain types of hernia might prove satisfactory for use in the reenforce-

ment of the abdominal wall. He found that the peritoneum has sufficient tensile strength so that it may be utilized in the repair of certain inguinal hernias. The experiments further show that peritoneum will unite with fascia and, when it comes in contact with the perimesian of muscle, will unite with it in a similar manner as does the fascial suture. The author suggests that the hernial sac, which now is discarded, be used in operations in which indications exist for reenforcement of the abdominal wall.

Selective Thoracoplasty in Treatment of Tuberculosis.—Overholt emphasizes that thoracoplasty should be so planned that maximal collapse of the involved lung and minimal collapse of the healthy portions of the lung is the result. The portion of the thoracic cage to be resected should not only include that part of the thoracic wall over areas of cavitation but should extend sufficiently to relax fibrotic uncavitated lung. The collapse obtained in the area treated should be complete within itself with each stage. In order to accomplish this, long or complete rib and transverse process resections should be carried out, beginning at the top of the thoracic cage. The length of time between stages should be long enough to allow an accurate estimation of the necessity for, and the extent of, a second rib resection. This period should also be of sufficient length to permit the patient to receive the maximal benefit from the first operation before the second one is attempted. The operation can be offered to patients with a relatively small amount of involvement of the upper portion of one lung, because the base on the same side is conserved. The operation can be offered to patients with bilateral disease who have good lower lobes and who otherwise would have no hope for recovery. Of 120 operations on seventy-three patients, the operative mortality was 2.5 per cent and the patient mortality 4.1 per cent.

Archives of Ophthalmology, Chicago

13: 1-150 (Jan.) 1935

Detachment of Retina: Treatment by Means of Pyrometric Electrode. L. Coppez, Brussels, Belgium.—p. 1.
Some Observations as to Indications for Advancement and Kindred Operations. P. C. Jameson, Brooklyn.—p. 3.
Association of Optic Neuritis, Facial Paralysis and Facial Hemiatrophy. E. A. Shumway, Philadelphia.—p. 8.
Hydrogen Ion Concentration of Tears: Its Relation to Certain Ocular Symptoms and Conjunctival and Corneal Lesions. G. N. Hosford and A. M. Hicks, San Francisco.—p. 14.
*Histologic Observations on Fundus in Leukemia. I. Goldstein and D. Wexler, New York.—p. 26.
Lectures on Motor Anomalies of Eyes: II. Paralysis of Individual Eye Muscles. A. Bielschowsky, Breslau, Germany.—p. 33.
Testing Eyes of School Children: New Eye Test Cabinet. W. L. Gould, Albany, N. Y.—p. 60.
Physiologic Optics of Retinoscopy. V. Johnson, Chicago.—p. 65.
Chemistry of Lens: VII. Growth and Senescence. A. C. Krause, Baltimore.—p. 71.
Reaction of Buffer Solution and of Ophthalmic Drugs: Further Note. S. R. Gifford, Chicago.—p. 78.

Histologic Observations on Fundus Oculi in Leukemia.—From their study of eleven eyes in cases of leukemia it appears to Goldstein and Wexler that in most instances the retinal lesions are minimal, since they do not produce profound disturbance in the retinal structure and the retinal vessels are normal in appearance. Such changes as marked sheathing of the veins, together with exudation of large numbers of leukocytes into the retina and nerve, are decidedly the exception. Also, fragmentation and necrosis of the walls of the larger vessels must be unusual. Similarly, in the choroid, while dilatation of the sinuses with leukocytes to a variable degree is the rule, the enormous infiltration with enlargement noted in one of the cases is exceptional. Destruction of the wall of the blood vessel following infiltration was noted. The fragments of the wall of the vessel were necrotic, and the only explanation is invasion or local proliferation of blood cells. Of unusual interest was the sheathing of the posterior ciliary vessels and the infiltration of large numbers of leukocytes into the episclera, both in association with the infiltration into the choroid. In this case exophthalmos and edema of the conjunctiva of the left eye had occurred more or less coincidentally with a marked increase in the white blood cell count. While the orbital tissues were not examined and orbital lymphoma therefore was not demonstrated, it is fair to assume, from the condition of the episclera, that such a lesion existed and was responsible for the edema and the exophthalmos. While it is possible that the sudden increase in the number of white blood cells was a factor in its etiology, the microscopic appearances do not warrant a definite statement as to whether the extra-ocular infiltration came by way of the choroid or directly from the blood stream.

Arch. of Physical Therapy, X-Ray, Radium, Chicago

16: 1-64 (Jan.) 1935

Radiothermy in Medicine. D. Kobak, Chicago.—p. 5.
Relationship of Occupational Therapy to Physical Therapy. W. R. Dunton Jr., Catonville, Md.—p. 19.
Production of Vasodilating Substances (Histamine and Acetylcholine) in Skin by Physical Therapy: Preliminary Report. K. Harpuder, New York.—p. 23.
Physical Therapy in Atrophic Rhinitis. F. Jouard, New York.—p. 28.
Therapeutic Hyperpyrexia Induced by Diathermy and Electric Blanket. S. H. Epstein and T. McHugh, Boston.—p. 32.
Manipulation in Low Back Conditions. H. H. Cox, Chicago.—p. 36.

Archives of Surgery, Chicago

30: 1-178 (Jan.) 1935

Therapeutic Use of Concentrated Streptococcus Serum of the New York State Department of Health in Patients with Infections of Ear, Nose and Throat. Adele E. Sheplar, Martha Jane Spence and W. J. MacNeal, New York.—p. 1.
Relationship of Infection to Postoperative Pulmonary Complications. W. D. Sutliff, Chicago, and B. F. Steele, Boston.—p. 14.
*Senile Osteomalacia: Report of Case. S. Kleinberg, New York.—p. 30.
*Preoperative Irradiation of Massive Tumors of Kidney: Clinical and Pathologic Study. L. R. Wharton, Baltimore.—p. 35.
Hemorrhagic Villous Synovitis of Knee Joint Due to Xanthoma: Report of Case. D. H. Kling, Los Angeles, and D. Sashni, New York.—p. 52.
Congenital Coxa Vara. I. Zadek, New York.—p. 62.
*Irradiation in Treatment of Tumors of Pituitary Gland: Report of Twenty-Three Cases. C. W. Rand and R. G. Taylor, Los Angeles.—p. 103.
Effect of Suprarenal Denervation and Splanchnic Section on Sugar Tolerance of Dogs. G. de Takáts and F. P. Cuthbert, Chicago.—p. 151.
Gastric Secretion: V. Achlorhydria Following Partial Gastrectomy for Ulcer: Studies with Histamine and Transplanted Gastric Pouch. E. Klein, New York.—p. 162.
Fifty-Fifth Report of Progress in Orthopedic Surgery. J. G. Kuhns, E. F. Cave, S. M. Roberts and J. S. Barr, Boston; J. A. Freiberg, Cincinnati; J. E. Milgram, New York, and R. I. Stirling, Edinburgh, Scotland.—p. 171.

Senile Osteomalacia.—Kleinberg cites a case of atrophy of bone in which the atrophy was limited to the spinal column and pelvis, the etiology was obscure, the softening of the vertebral bodies resulted in a painful posterior curvature of the spine and rest on a convex frame yielded complete relief. Clinical examination revealed no neurologic disturbances in the cerebrospinal system that could induce atrophy of bone. Disuse was dismissed because despite the pain the patient was able to get about considerably, walking and working every day. Thus it was concluded that the disease of the spine was nutritional or metabolic. The demineralization progressed to such a degree that it caused a partial collapse of certain of the dorsal vertebrae, with resultant pain and deformity. The nutritional upset may be considered a senescent degenerative change. Why the metabolic upheaval should appear and involve a limited portion of the skeleton is inexplicable. In addition to rest on the canvas convex frame the patient received sedative doses of baking and massage of the back several times a day. Within three weeks the pain and tenderness disappeared, the kyphosis was reduced, and the patient, with the support of a light plaster-of-paris jacket, was able to move about comfortably and was discharged.

Preoperative Irradiation of Massive Tumors of Kidney.—In the experience of Wharton, preoperative irradiation of both Wilms and Grawitz tumors causes a remarkable decrease in their size and makes them easily operable. Preoperative irradiation also causes definite cellular changes in the malignant tissue, such as hyalinization, pyknosis, fragmentation and destruction of the architecture of the tumor. Irradiation, however, will not destroy malignant tumors entirely. After having been intensively irradiated, tumors that he has removed have uniformly shown living malignant tissue; those that he has not removed have resumed active growth. Roentgen therapy is only a means of preparation to make the tumor operable, or a palliative measure to hold in check a tumor that cannot be removed. He believes that the transperitoneal approach is the most logical, clean and surest way to remove tumors of the kidney.

Irradiation in Treatment of Tumors of the Hypophysis.—Rand and Taylor studied twenty-three cases to estimate the value of high voltage radiation in the treatment of tumors of the hypophysis. There were five cases of chromophil adenoma, thirteen chromophobe adenomas, two adenocarcinomas and three cystic chromophobe adenomas. Chromophil adenomas react most favorably to this form of treatment. The permanence of relief is indefinite. Eosinophilic and basophilic cells seem to react most favorably to irradiation. Chromophobe adenomas have not responded uniformly. Tumors of the hypophysis may be mixed. The predominating cells may be of the chromophobe type, but there may be a smattering of other types of cells. Adenocarcinoma of the hypophysis apparently does not react favorably to high voltage irradiation. Cystic adenomas of the chromophobe variety show no improvement following irradiation. When apparent chromophobe tumors fail to react favorably to irradiation within a short time, they are likely cystic and more amenable to surgical treatment. Irradiation can be given more intensively if a decompression is provided first. Apparently certain patients suffering from pituitary tumors gain from moderate to useful vision following irradiation. Without irradiation they would almost certainly become blind. No definite regression has been seen in general acromegalic symptoms following irradiation nor any definite advance in symptoms. Postoperatively, patients without irradiation have maintained improved vision on an average of from one to three years. It would seem logical in selected cases to employ irradiation first, in the hope that certain patients may be helped enough thereby to render surgical intervention unnecessary. These patients should be under the close scrutiny of a neurologic surgeon, for, at best, high voltage irradiation will give satisfactory results in only a certain proportion of cases. It does not replace the surgical procedure but rather acts as an adjunct to it.

Florida Medical Association Journal, Jacksonville

21: 269-322 (Jan.) 1935

Recent Progress in Aviation Medicine. L. Iverson, Pensacola.—p. 279.
Practical Points in Osteomyelitis, as Seen at the American Legion Hospital for Crippled Children at St. Petersburg. P. Le Breton, St. Petersburg.—p. 283.
Bronchial Asthma. R. L. Cline, Lakeland.—p. 289.
Value of Hormones as Diagnostic Agents. C. D. Hoffman, Orlando.—p. 291.

Georgia Medical Association Journal, Atlanta

24: 1-40 (Jan.) 1935

Typhus Fever: Endemic Typhus Fever in Georgia. M. S. Dougherty Jr., Atlanta.—p. 1.
Id.: Recent Developments in Knowledge of Endemic Typhus Fever. T. F. Sellers, Atlanta.—p. 7.
Breast Lesions. W. P. Nicolson Jr., Atlanta.—p. 14.
Medical Aspects of Some Acute Abdominal Conditions. S. C. Ketchin, Louisville.—p. 19.
Carcinoma of Abdominal Testicles: Report of Two Cases. W. P. Harbin and L. Harbin, Rome.—p. 24.

Johns Hopkins Hospital Bulletin, Baltimore

56: 1-60 (Jan.) 1935

Experimental Approach to Cancer Problem: I. Four Important Phases of Cancer Research: II. Avian Tumors in Relation to General Problem of Malignancy. J. B. Murphy, New York.—p. 1.
*Thirty Minute Spectrographic Micromethod for Detection of Pathologic Lead in Peripheral Blood. H. Blumberg and T. F. M. Scott, Baltimore.—p. 32.
Demonstration of Encephalic Control of Micturition by Electrical Stimulation. O. R. Langworthy and L. C. Kolb, Baltimore.—p. 37.
Iron of Blood: Comparison of Values for Hemoglobin Determined by Newcomer Method and Calculated from Iron Content. H. W. Josephs, Baltimore.—p. 50.

Detection of Lead in Peripheral Blood.—Blumberg and Scott describe a thirty minute spectrographic micromethod for the detection of pathologic amounts of lead in 0.1 cc. samples of peripheral blood. The instrument used was a Hilger E1 large quartz spectrograph, operated in conjunction with a graphite arc and a quartz spherocylindric concentrating lens. The electrodes employed were high purity graphite rods, 10 mm. in diameter. The upper electrode, the negative, was used with a flat surface. The lower electrode, the positive, was hollowed at its upper end by means of a steel drill, leaving an evenly cored space approximately 6.5 mm. in diameter and 3 mm. in depth. For each analysis three samples of blood from the finger were obtained, preferably from different fingers. The samples were collected in 0.1 cc. micro blood sugar pipets. The blood from each finger was delivered immediately into the hollow core of a prepared electrode, which was then replaced in the inverted test tube and taken for analysis. By means of careful drainage, the pipets were emptied so well that the amount of blood left adhering to their walls was of no practical significance. With the blood in the core of the lower positive electrode, and with the flat upper electrode as the negative pole, the arc was struck. For about fifteen seconds the electrodes were scarcely separated, thus permitting the clotted blood to smolder and partly to char, without actually burning. The electrodes were then drawn apart and the arc allowed to burn. By visual observation of the light beam and of the burning electrodes, it was easy to tell when the sample had completely burned. This usually required from thirty to forty-five seconds. After the photographic plate was developed and fixed, it was rinsed in water and examined. If the blood contained a pathologic amount of lead, the sensitive lead line at 2,833.07 angstrom units would appear visible to the eye, and the minor lines at 2,802.09 angstrom units and 2,614.20 angstrom units could be seen with the aid of a lens. This was considered a positive result. In the control samples the sensitive line at 2,833.07 angstrom units either did not appear or showed as a faint line visible only with the aid of a lens. The minor lines could not be detected at all. This was considered a negative result. The authors originally intended the method for peripheral blood samples, but it can be used also with uncoagulated venous blood. In the case of the latter, care must be taken to use an anticoagulant free from lead. In their experience it has appeared that, unless a preliminary drying of the measured sample is resorted to, the uncoagulated venous blood is more difficult to burn than the quickly clotting peripheral sample.

Journal of Allergy, St. Louis

6: 111-214 (Jan.) 1935

*Effect of Low Relative Humidity at Constant Temperature on Pollen Asthma. B. Z. Rappaport, T. Nelson and W. H. Welker, Chicago.—p. 111.
Air Studies at Higher Altitudes. E. L. MacQuiddy, Omaha.—p. 123.
Pollen Content of Air in North America. O. C. Durham, North Chicago, Ill.—p. 128.
Pathology of Two Fatal Cases of Bronchial Asthma. P. P. Michael and A. H. Rowe, Oakland, Calif.—p. 150.
Physical Allergy: Its Rôle as Manifested in Routine Study of Three Hundred and Twenty-Five Consecutive Allergic Cases. O. Swineford Jr., University, Va.—p. 175.
*Technic on Intracutaneous Tests and Results of Routine Tests in Normal Persons. F. M. Rackemann and F. A. Simon, Boston.—p. 184.
Status Asthmaticus. A. T. Sterling, Philadelphia.—p. 189.

Effect of Low Humidity on Pollen Asthma.—From a study of the results of twenty-two patients, sixteen of whom were completely relieved in four days, Rappaport and his associates conclude that the rapidity with which pollen asthmatic patients are relieved is greater under conditions of low humidity and relatively constant temperature in a pollen-free atmosphere than when the temperature and humidity are not controlled. In a pollen-free atmosphere, with the relative humidity ranging between 15 and 40 per cent and the temperatures ranging between 72 and 82 F., patients with pollen asthma had a delayed onset (from six to eight hours) of symptoms in attacks precipitated by storms. This conclusion is based on a comparison with the time of onset (one hour) of symptoms in the patients of an experimental ward in 1932. It is the authors' impression that the asthmatic attacks in the ward during storms were less severe and that the symptoms disappeared much more rapidly as compared to attacks precipitated during the experimental period of 1932. Under their experimental conditions, a concentration of ozone considerably greater than occurs after a heavy electrical storm showed no beneficial or detrimental effects. Some other factor, or factors, outside of pollen, humidity, temperature, or the concentration of ozone must play a part in the precipitation of symptoms of asthma in pollen asthmatic persons. Barometric changes and ionization have not been studied.

Technic on Intracutaneous Tests.—Rackemann and Simon emphasize the importance of chemical as well as bacteriologic

cleanliness in making intracutaneous tests. The need for all-glass syringes is defined, and a convenient rack for segregating and labeling the syringes is described. When this improved technic is applied to the study of normal, nonallergic individuals, many positive skin tests are obtained. The importance of this observation to the study of allergic patients is discussed.

Journal of Lab. and Clinical Medicine, St. Louis

20: 337-450 (Jan.) 1935

Meteorologically Conditioned Variability of Serologic Tests in Syphilis. E. T. Hoverson, Kankakee, Ill., and W. F. Petersen, Chicago, with technical assistance of D. Sackett, Elgin, Ill.—p. 337.
*Creatinine Clearance During Hyperthermia of Diathermy and Fevers. W. H. Grant and Grace Medes, Minneapolis.—p. 345.
Effect of Alcohol on Spleen Volume. F. D. McCrea, D. F. Marion, W. W. Tyson and W. P. Kavanagh, Durham, N. C.—p. 350.
Some Studies on Etiology of Granuloma Inguinale. H. A. Poindexter, Washington, D. C.—p. 353.
Stereoscopic Roentgenography of Bedridden Pneumonia Patients. P. C. Hodges and T. H. Lipscomb, Chicago.—p. 357.
*Response to Infection in Bone Marrow Dyscrasias. F. H. Bethell, Ann Arbor, Mich.—p. 362.
*Elliptic Human Erythrocytes: Observations of Size, Volume and Hemoglobin Content. D. J. Stephens and A. J. Tatelbaum, Rochester, N. Y.—p. 375.
Colloidal Gold Reaction in Five Hundred Cases of Neurosyphilis. W. C. Menninger, Topeka, Kan., and L. Bromberg, Chicago.—p. 383.
Comparison of Various Concentrations of Sodium Oxalate Solution with Heparin for Determination of Packed Cell Volume. O. S. Walters, St. Louis, and J. W. May, Lawrence, Kan.—p. 385.
Occurrence of Eggs of Heterodera Radicicola in Human Feces. A. E. Keller, Nashville, Tenn.—p. 390.
Virus of Lymphogranuloma Inguinale: Its Cultivation, Its Antigenic Value as Vaccine and Also in Production of Antiserum. J. T. Tamura, Cincinnati.—p. 393.
Water Studies in Obesity. E. C. Bartels, Springfield, Ill., and B. Blum, Rochester, Minn.—p. 401.
*Modified Method for Determination of Blood Cholesterol. J. E. Andes, New Orleans.—p. 410.
Enumeration of Blood Platelets. I. Olef, Boston.—p. 416.
Valves Versus the Motor Blower in the Benedict Type of Metabolism Apparatus Now in Common Use. P. Roth, Battle Creek, Mich.—p. 436.

Creatinine Clearance During Hyperthermia.—Grant and Medes studied the creatinine clearances in dogs during the hyperthermia produced by diathermy and creatinine clearances in patients with fever caused by infection in order to determine the effect of general systemic hyperthermia on creatinine clearance and the extent to which any changes observed in infectious fevers may be referred to the elevation of body temperature. In contrast to the general parallelism that exists between body temperature and creatinine clearance in dogs during diathermy when all other factors are being held as nearly constant as possible, the creatinine clearances in patients with fever undergo wide variations. In the series of fifteen patients observed, the clearances during the height of the fever varied from 600 to 60 per cent of their postfebrile values. A survey of the relationship between blood pressure and filtration during the fever revealed similar irregularities: Nine patients showed an elevation of all three factors, temperature, blood pressure and filtration; three showed an increase in blood pressure with a fall in filtration, and in one patient filtration and blood pressure were lowered, while in the remaining two cases the changes in blood pressure and filtration were insignificant. The group whose behavior is the most difficult to explain on a theoretical basis is that in which blood pressure and temperature were both elevated while filtration was lowered. Two other known factors may be considered as responsible for this behavior: (1) There may be a decrease in the volume flow of blood to the kidney in spite of an elevation of temperature and blood pressure, and (2) there may be a direct effect of the infection on the kidney, resulting in a temporary closing off of some of the glomeruli or in an altering of their permeability.

Response to Infection in Bone Marrow Dyscrasias.—Bethell hopes that, by observing the degree of bone marrow response as measured by the total neutrophil count, the effort of the response as indicated by the percentage of immature forms and the severity of the infection as interpreted by the percentage of basophilic granule cells, some information may be gained concerning the physiology of the bone marrow in certain pathologic states. He observed that the response of the bone marrow to infection is dependent on its preexisting functional state as well as on the nature and severity of the infectious process. The estimation of the number of neutrophils in the circulating blood and their classification into nonfilament and filament nuclear forms does not differentiate between the intrinsic and extrinsic factors involved in the response. The occurrence of basophilic granules in the cytoplasm of the neutrophils is, on the other hand, solely a result of the infection. The total neutrophil count may be regarded as a measure of the degree of the bone marrow response, the percentage of nonfilament or immature forms as an indication of the effort of the response, and the percentage of neutrophils exhibiting basophilic granulation as a sign of the severity of the infection. By correlation of these data, obtained from successive blood examinations of the same subject, it is possible to ascertain the nature of the bone marrow response as well as the progress of the infection. The author presents six cases of infection in the presence of various types of bone marrow dyscrasia which illustrate the manner in which this correlation is carried out. In these cases the percentage of neutrophils exhibiting cytoplasmic basophilic granulation gives a more accurate indication of the severity and the progress of the infection than either the total number of neutrophils per cubic millimeter or their degree of immaturity. Of the four fatal cases presented, pathologic diagnoses were available in three, and, so far as the methods of examination permitted, the conclusions arrived at by the blood studies were confirmed.

Elliptic Human Erythrocytes.—Stephens and Tatelbaum discuss the hematologic studies of fifteen members of an Italian family, eight of whom exhibited elliptic erythrocytes. In each of the affected persons there was an increase in the number of red blood cells per cubic millimeter, with a definite decrease in the mean corpuscular volume and the mean corpuscular hemoglobin. The number of red blood cells was inversely proportional to the mean cell volume and hemoglobin content. Two dimensional measurements of cells in fixed, stained smears indicated that the decrease in size involved the round cells and the abnormally shaped cells to approximately the same extent, without increase in the variability of distribution of cell size. In the unaffected members of the family the erythrocytes were normal in shape, size, volume and hemoglobin content.

Determination of Blood Cholesterol.—Andes states that, in the colorimetric estimation of blood (or serum) cholesterol, plaster of paris seems to be the most satisfactory desiccating medium and chloroform appears to be the most suitable extracting medium. He describes a method for the determination of cholesterol in blood (or other body fluids). The blood is dried on plaster of paris and the cholesterol is extracted with chloroform, the entire extraction and color development being completed in a Folin-Wu sugar tube.

Journal of Pediatrics, St. Louis

6: 1-150 (Jan.) 1935

Celiac Disease (Chronic Intestinal Indigestion): Report of Three Cases with Autopsy Findings. J. H. Hess and O. Saphir, Chicago.—p. 1.
Athletic Performance as Function of Growth: Speed in Sprinting. H. Gray and F. J. Daly, San Francisco.—p. 14.
Hemorrhage and Subsequent Calcification of Suprarenal. C. E. Snelling and I. H. Erb, Toronto.—p. 22.
Chorea: Is It a Manifestation of Rheumatic Fever? J. R. Gerstley and S. A. Wile, Chicago; E. I. Falstein, Elgin, Ill., and May Gayle, Houston, Texas.—p. 42.
*Occurrence of Blood-Filled Cysts on Cardiac Valves in Infancy. S. D. Mills, Rochester, Minn.—p. 51.
*Sodium Thiocyanate in Prophylaxis and Treatment of Bacillary Dysentery, with Especial Emphasis on the Shiga Type: Progress Report Covering First Two Year Period of Clinical Study. E. C. Mitchell and D. W. Goltman, Memphis, Tenn.—p. 57.
Pulmonary Lesions Associated with Intra-Uterine Asphyxia. M. Rosenthal, Brooklyn.—p. 71.
Gonorrheal Vaginitis in Children Treated by Diathermy: One to Three Year Follow Up. R. J. Crossen, St. Louis.—p. 82.
*Continuous Intravenous Therapy in Infants. J. E. Ashby and H. L. Moore, Dallas, Texas.—p. 88.
Hydrocephalus of Unusual Size. D. J. Dolan and M. J. H. Grand, New York.—p. 94.

Blood-Filled Cysts on Cardiac Valves in Infancy.—Mills states that the routine postmortem examinations of seventy-two hearts of new-born infants and children during a period of six months disclosed the rather frequent occurrence

of small, blood-filled elevations on the auricular surfaces of the atrioventricular valves. Twenty-three, or 32 per cent, disclosed the presence of blood-filled cysts on the cardiac valves. The majority of the subjects were full-term infants who had either been stillborn or had died within the first week of life. The oldest child of the group with cysts on the cardiac valves was 8 months of age; the youngest, a premature infant in the seventh month of gestation. Although the largest number of cysts (fourteen) occurred in the case of this premature infant, none were found in a group of five hearts from fetuses 6 months old or less when the cardiac valves were studied microscopically in serial section. The causes of death in the entire series were principally trauma at birth, congenital malformations or infection among older children. The site of predilection for these nodules is the atrioventricular valves, with the tricuspid valves slightly the favorite. The presence of a blood-filled cyst also was noted on a papillary muscle in one case. These cysts usually are found from 1 to 3 mm. removed from the free edges of the valve on its auricular surface, although they may occur anywhere on the surface of the leaflets. It is usual for these cysts to be multiple, and occasionally they may be grouped so closely that the surface of the valve resembles a raspberry. Cysts on the semilunar valves project on the ventricular aspect of the valve near the base of the cusp. The cysts vary in size from that of a pinpoint to 2 mm. in diameter. They may be multilocular, and this is particularly apparent when they are seen microscopically. Grossly, they appear as dark, sharply circumscribed, rounded elevations on the smooth surface of the valve. They are easily visible in a good light with the naked eye because of the contrast of the dark contents of the cyst against the pale background of the surface of the valve. The cyst usually is a round, smooth-walled cavity, pushing up the endothelium of the surface of the valve beneath which it lies. The wall is composed of a few concentric layers of fibrous connective tissue, and the lining of the cyst is made up of a single layer of spindle shaped cells with long, oval nuclei that cannot be distinguished from endothelium. The cysts may be multilocular or a series of communicating cavities. If the pressure within them becomes too great, the partitions may rupture, thereby converting a group of cysts into one large cavity. Small outpouchings from the periphery of the wall of the cyst, generally on the ventricular side, may be seen. In addition, several small, oval or elongated spaces are seen, which apparently are lined with endothelium, lying within the substances of the valve and running in a direction at right angles to the long axis of the leaflet. The contents of the cysts are chiefly erythrocytes, with occasional leukocytes and cells desquamated from the inner wall of the cavity. The explanations that have been offered by Elsasser, Berti, Nichols, and Haushalter and Thiry for the origin of these cysts are discussed and the present theory is given that they are cystic dilatations at the ends of endothelial-lined canals in the substance of the valves.

Sodium Thiocyanate in Treatment of Bacillary Dysentery.—Mitchell and Goltman observed that sodium thiocyanate in the dosage of one-third grain (0.02 Gm.) per kilogram of body weight orally seems to have definite prophylactic value in Shiga dysentery and also if given intravenously in the dosage of 20 mg. per kilogram of body weight on successive days within twenty-four hours after onset in Shiga dysentery. It does not appear to influence dysentery due to other strains. However, these types of dysentery are usually mild in onset and in all the authors' work have been in progress several days before being seen. The drug does not influence either the course of the disease or the mortality when it is given as late as thirty hours after onset. It is probably of little value when given after twenty-four hours. When the drug is given early, not later than twenty-four hours after onset, it has a decided value in influencing the mortality and the severe toxic course of Shiga dysentery. The mortality with the new treatment in the charity services has not shown a material improvement over previous years. This is attributable, in the authors' judgment, to the fact that the cases in such services are rarely seen until the disease has been in progress for more than twenty-four hours. In the Osceola epidemic (private cases) in which the drug was administered at the first appearance of diarrhea, only one patient in twenty-six died. The effectiveness of sodium thiocyanate therapy clearly depends on its early use. No claim for sodium thiocyanate (rhodanate) as a specific, either in the prevention or in the treatment of bacillary dysentery, is made by the authors as a result of their clinical experience. Their preliminary results, however, lead them to believe that their method of treatment is worth further trial, and they hope to publish at a later date a much more complete clinical report in which a larger number of institutions and physicians have participated.

Continuous Intravenous Therapy in Infants.—Ashby and Moore have found the scalp by far the most logical site for the continuous administration of a solution in the vein, because (1) the blood vessel is stable, (2) the application is easy, (3) the patient may move or toss the head, the arms and legs being free, and (4) the vessels in this area are the smallest. It is their contention that the greatest difficulty in the use of continuous intravenous administration, i. e., clogging of the needle or cannula by blood, is thus overcome. Many small tributaries of the superficial temporal veins draining the parietal and frontal aspects of the scalp are found in addition to the two or three small tributaries of the frontal and supra-orbital veins, which drain the anterior part of the scalp and flow down over the middle of the forehead. The latter vessels are the authors' first choice, because the child can roll his head from side to side without interfering with the flow of the solution. The infusion is given entirely by gravity. The container is an ordinary 300 cc. arsphenamine tube, connected by a short piece of rubber tubing to a drip bulb, commonly known as the rectal drip, from which a piece of rubber tubing from 3 to 4 feet in length passes to a small glass adapter half an inch in length. The needle, a 28 gage one-half inch so-called tuberculin needle, fits the adapter. The container hangs on the hook of a standard, adjustable in height. This adjustability regulates the rate of flow, which also may be regulated by a screw clamp inserted anywhere between the drip bulb and the needle. The needle may be kept in the vein most efficiently by a 3-inch strip of adhesive tape, 2 inches wide. This is placed firmly over the needle, adapter and skin directly in front of the needle. A small piece of cotton is placed under the adapter. In case of movement of the scalp, the skin, vein and needle move together without disturbing the flow. The rate of flow is judged by the number of drops per minute; this varies from 5 to 30 drops. The first 200 or 300 cc. is allowed to enter the vein at a rate of from 15 to 20 drops per minute, and then the rate of flow is usually reduced to 10 or 12 drops per minute and regulated according to the heart rate, the beginning of diuresis and the clinical appearance of the patient. The solution at ordinary room temperature is regarded as safe. The authors give blood transfusions in the same small blood vessels with the same sized needle. Their transfusion apparatus does not include the drip bulb, but a three way stopcock is inserted. The blood is drawn from the arsphenamine tube into a syringe fitting the stopcock; the valve is turned and the blood injected into the vein slowly. Citrated blood, which is strained when placed in the container, is used. Obstruction of the needle is rare. The authors have employed this procedure in 511 cases.

Maine Medical Journal, Portland

26: 1-14 (Jan.) 1935

Evolution of the Medical Examiner and His Present-Day Problems. W. E. Freeman, Yarmouth.—p. 3.

Routine Hospital Laboratory Examinations. M. Warren, Portland.—p. 9.

Some Facts About Wright's Stain. J. T. Fitzgerald, Portland.—p. 10.

Medical Annals of District of Columbia, Washington

4: 1-28 (Jan.) 1935

Malaria Treatment of Neurosyphilis. W. Freeman, Washington.—p. 1.

The General Practitioner's Concept of Treatment of Arthritis. W. M. Yater, Washington.—p. 4.

Tendon Transplantation for Paralysis of External Rectus Muscle: Report of Case. E. L. Goodman, Washington.—p. 11.

Empyema of Ureteral Stump: Report of Case. R. M. LeComte, Washington.—p. 13.

Dermatologic Conditions Encountered by the Otolaryngologist and Ophthalmologist. C. B. Campbell, Washington.—p. 14.

Medical Bull. of Veterans' Adm., Washington, D. C.

11: 77-184 (Oct.) 1934

Intrathoracic Changes in Tularemia. A. Blumberg and R. L. Russell.—p. 77.
Diagnosis of Pleuropulmonary Disease. H. B. Williams.—p. 84.
Cardiac Neuroses. C. H. Ketterer.—p. 94.
Spinal Anesthesia. H. E. Bundy.—p. 99.
Pernicious Anemia wtih Combined Sclerosis. D. L. Liberman.—p. 102.
Surgical Use of Ultraviolet Irradiated Mineral Oils. N. H. Matros and J. D. Brooks.—p. 106.
*Relationship of Influenza and Epidemic Encephalitis. J. H. Hurst.—p. 110.
Weak or Flat Feet. E. E. Hobby.—p. 135.
Transillumination in Orchitic Atrophy. H. A. Brady.—p. 138.
Therapeutic Value of Music for Psychotic Patients. A. H. Pierce.—p. 142.
Beneficial Effects of Music for the Mentally Ill. W. G. Richter.—p. 148.

Relationship of Influenza and Epidemic Encephalitis.—Hurst's study reveals that epidemic encephalitis is an acute disease with an incubation period of about ten days, spreading slowly from site to site and tending to persist for a considerable time in the locality affected. In certain cases the infection is through open-skin lesions; it affects men more than women and attacks parts of the central nervous system, especially the basal ganglions. It has a relationship to herpes which is interesting in view of the predilection of that disease for the posterior root ganglions of the spinal cord. The fact that herpes appears in some cases of influenza is of interest but is not sufficient to warrant claim of a common entity for the two diseases in the face of convincing evidence to the contrary. Epidemic encephalitis lacks the catholicity of infection, rapidity of spread and brief duration as a disease, and, as an epidemic, the chest attack and the characteristic course, complications and sequels of influenza. The evidence fails in any particular to indicate a common entity for influenza and epidemic encephalitis. It fails to indicate that the presence of influenza predisposes to encephalitis, either in the mass or in the individual. The cases diagnosed as influenza at the time of onset in an epidemic which later require a correction of diagnosis to encephalitis are extremely rare. The possibility must be admitted for cases that within a year or two after a disease diagnosed as influenza show unmistakable permanent residuals of epidemic encephalitis—such as masked face, parkinsonian tremor, festinating gait and speech defect with or without mental changes sometimes found in this disease—provided that in the interval there has been no showing of any intercurrent disease which, in sound medical judgment, could be interpreted as epidemic encephalitis.

Military Surgeon, Washington, D. C.

76: 57-112 (Feb.) 1935

Stopping Power. C. Goodard.—p. 57.
Sabin's Immediate Pneumococcus Typing and Its Value to Small Station Hospitals. S. White.—p. 72.
Looking Backward. H. W. Jones.—p. 74.
Medical Reserve Trains at the Mayo Clinic, Oct. 7 to 21, 1934. T. M. Carow.—p. 84.
Analysis of Physical Examinations for the Civilian Conservation Corps at Richmond, Virginia, Oct. 1 to 15, 1934. N. Mercer.—p. 88.

Nebraska State Medical Journal, Lincoln

20: 41-80 (Feb.) 1935

Analysis of Goiter Cases at the University Hospital. C. E. Gurney, Omaha.—p. 41.
Thyroid Heart: Its Problems and Treatment. M. C. Anderson, Omaha.—p. 44.
Persistent Hyperthyroidism: Case Reports. J. D. Bisgard, Omaha.—p. 46.
Hyperplastic Goiter with Temporary Cardiac Changes: Case Studies in Goiter, Number Seven. A. Brown, Omaha.—p. 50.
*Management of Thyroid Malignancies. N. F. Hicken, Omaha.—p. 52.
Struma Lymphomatosa (Hashimoto): Report of Ninth Case. C. Emerson, Lincoln.—p. 58.
Progress of Surgery: Review of Literature for Last Six Months of 1934. H. H. Davis, Omaha.—p. 60.
Diagnostic Therapeutics in Gastro-Intestinal Conditions. F. W. Heagey, Omaha.—p. 63.
Induction of Labor. L. S. McGoogan, Omaha.—p. 67.

Management of Malignant Conditions of Thyroid.—In determining the efficacy of surgical and radiation therapy, Hicken studied 264 cases of malignant disease of the thyroid. The radiosensitive tumors are the lymphosarcomas, the malignant adenomas and the papillary adenocarcinomas. Those which do not respond to either the interstitial or roentgen therapy are the spindle cell sarcomas, the carcinoma-sarcomas and the scirrhous carcinomas. Biopsies should be made of every suspected malignant goiter, for the amount of radiation given depends on the type of neoplasm encountered. Complete removal of the neoplasm is always to be desired. Partial excision of the major portion of the infiltrating tumor, cervical decompressions, tracheotomies and biopsies are valuable surgical adjuncts. A combination of surgical and roentgen therapy is more effective than either agent alone. Recurrent malignant lesions should always be excised and the local areas submitted to intensive irradiation. Metastatic lesions offer no contraindications to active surgical and roentgen therapy. The malignant adenoma comprises 90 per cent of all thyrogenic malignant cases and gives an excellent response to surgical and roentgen treatments. Pessimism and apathy have no place in the treatment of malignant goiters.

New England Journal of Medicine, Boston

212: 87-136 (Jan. 17) 1935

Vaginal Hysterectomy. O. N. Eastman, Burlington, Vt.—p. 87.
Gynecologic Problems of Interest to the Surgeon in General Practice. A. H. Morse, New Haven, Conn.—p. 90.
What Is Wrong with the Patient Who Feels Tired, Weak and Toxic? W. C. Alvarez, Rochester, Minn.—p. 96.
Mesenteric Thrombosis. W. J. P. Dye, Wolfeboro, N. H.—p. 105.
Prevention or Postponement of Death from Heart Failure. C. S. Burwell, Nashville, Tenn.—p. 108.

212: 137-182 (Jan. 24) 1935

Agranulocytosis: Its Etiology and Treatment. H. Jackson Jr. and F. Parker Jr., Boston.—p. 137.
Bleeding Gastric Ulcer. G. A. Moore, Brockton, Mass.—p. 149.
*Typical Epileptic Seizures in Course of Schizophrenia: Report of Two Cases. E. F. Falsey, New Haven, Conn.—p. 153.
Primary Carcinoma of Vagina. J. T. Williams, Boston.—p. 156.
General Considerations and Principles of Excretion Urography. M. Swick, New York.—p. 158.

Epileptic Seizures in Course of Schizophrenia.—Falsey presents two cases of typical epileptic seizures in the course of schizophrenia. Both instances occurred in young persons in whom arteriosclerotic and syphilitic factors may be definitely ruled out as possible etiologic factors in the pathogenesis of the seizures. In each instance the seizures were typically epileptic and occurred for the first time during a catatonic exacerbation of a rather long standing schizophrenia. In neither instance have the seizures recurred since the acute catatonic phase of the psychosis has subsided. In one case there was a mild infection (nasopharyngitis) and a mild elevation of nonprotein nitrogen (44.4 mg. during the period of epileptic manifestations). It appears that the epileptic seizures were either released by the catatonic episodes or were the result of the same etiologic factors involved in the exacerbation of the psychosis. Thus they appear to be a reflection of deep-seated vegetative, metabolic or psychobiologic changes, which not only were concomitant with the psychosis but so lowered the convulsive threshold that epilepsy appeared.

Public Health Reports, Washington, D. C.

50: 37-70 (Jan. 11) 1935

Incidence of Amebic Dysentery in New York City: Note. R. Olesen and J. Rosenbluth.—p. 37.
Effect of Experimental Local Irritation on Susceptibility to Vaccine and Encephalitis Virus (St. Louis Type). C. Armstrong.—p. 43.
Blood Cholesterol in Leprosy: Study of Total and Free Cholesterol, Cholesterol Esters, Van den Bergh Reaction and Complement Fixation Test. S. H. Black and H. Ross.—p. 50.

50: 71-94 (Jan. 18) 1935

Rat and Rat Flea Survey of Los Angeles Harbor. H. E. Trimble and G. C. Sherrard.—p. 74.
Administrator's Point of View of Psychiatric Services in Correctional Institution. J. W. Sanford.—p. 79.

Yale Journal of Biology and Medicine, New Haven

7: 191-274 (Jan.) 1935

Psychiatrists, Neurologists and the Neurosurgeon. H. Cushing, New Haven, Conn.—p. 191.
Clinical Diagnosis of Dissecting Aneurysm of Aorta. J. B. Lounsbury, New Haven, Conn.—p. 209.
Psychoses Complicating Other Diseases. E. Kahn, New Haven, Conn.—p. 215.
Commentary on Recent Advances in Clinical Obstetrics. H. Thoms, New Haven, Conn.—p. 225.
Nature and Origin of Proteins. R. J. Block, Scarsdale, N. Y.—p. 235.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Physical Medicine, London

9: 157-176 (Jan.) 1935

The Young Male Athlete. R. Cove-Smith.—p. 159.
The Young Woman Athlete. Louise McIlroy.—p. 161.
Treatment of Paralysis Due to Spinal Injury. E. L. Gowlland.—p. 162.
Manipulative Surgery in Athletic Injuries. W. E. Tucker.—p. 164.
Rider's Strain: Notes on Muscle Strain in General. M. Smart.—p. 166.
The Car and Its Driver: Some Observations on Driving Posture. M. E. Ormsby.—p. 170.
Infra-Red and Ultraviolet Irradiation of Injuries in Sport. W. A. Troup.—p. 172.

British Journal of Radiology, London

8: 1-64 (Jan.) 1935

*Protection of Radium Workers from Gamma Radiation. G. W. C. Kaye, G. E. Bell and W. Binks.—p. 6.
Tissue Culture: I. Advantages and Limitations as Research Method. H. B. Fell.—p. 27.
Alteration in Sensitivity of Cells Toward Radiation Produced by Cold and by Anaerobiosis. J. C. Mottram.—p. 32.
Time Intensity Factor in Relation to Genetic Effects of Radiation. H. D. Griffith and K. G. Zimmer.—p. 40.
*Simple Method of Sinus Radiography in Erect Posture. J. S. Fulton.—p. 48.
Syringe for Intra-Oral Administration of Lipiodol. J. Raffan.—p. 52.

Protection of Radium Workers from Gamma Radiation.—Kaye and his associates studied experimentally the two main factors of gamma-ray protection, viz., remoteness and lead shielding. The minimal shielding and the tolerance working distance have been determined under various conditions on the assumptions of a daily tolerance dose of 0.2 roentgen and a Sievert gamma-ray unit "dose" of 8 roentgens. The results are also calculable in simple cases from the lead transmission curve of gamma rays, which has also been determined under conditions taking full account of scattering. The results lend support to the recommendations of the International and British Committees for X-Ray and Radium Protection and furnish evidence that the recommendations provide a reliable basis for radium protection, particularly on such points as radium storage, the employment of temporary workers and the importance of expeditious manipulation in busy radium centers.

Method of Sinus Roentgenography in Erect Posture.—Fulton submits a method for examining the nasal accessory sinuses in the erect posture, which permits the use of a focal film distance of 4 or 5 feet. The rigid alinement of the x-ray tube and the film permits the use of the smallest possible cone. With a small aperture cone good roentgenograms may be obtained without the use of a Potter-Bucky diaphragm, and the object film distance can thus be reduced to a minimum. For those who desire still further to eliminate scattering it is simple to incorporate a Lysholm grid without much increasing the object film distance. The method permits the taking of four projections on a single 15 by 12 inch film. The apparatus consists of a tube stand, a special caset frame and a telescopic stool. X-rays reach the caset only through a circular aperture, 5½ inches in diameter, which is cut in the center of the frame. Thus, with the caset pressed into each of the four corners in turn, four circular images are obtained on the film, each being 5½ inches in diameter, the centers of these being 6 inches apart. In the subsequent blackening of the surrounding film, the images are cut down to have a diameter of 5 inches in order to allow for any slight error in the centering of the cone. The provision of a rigid head clamp is essential. The most suitable seat for the patient is one in which the height may be varied by the roentgenographer while the patient remains seated. The usual procedure is adopted in fixing the patient's head. In the mentovertex projection, the patient turns round and faces the tube, thus bringing the right side to the left. To preserve a uniform relationship on the film, the caset is turned upside down for this exposure. Generally, 240 milliampere seconds and a kilovoltage between 55 peak kilovolts for the lateral and 75 peak kilovolts for the mentovertex projection in the average patient are employed. This energy can be delivered through a 2½ kilovolt tube. When the four exposures have been made, the surrounding film is blackened by giving it a light exposure at low kilovoltage through a masking board, which consists of three layers of three-ply wood. In the center layer the wood is replaced in parts by four disks of 8 pounds of lead, 5 inches in diameter, so placed that they protect the four circular roentgenograms. Embedded in this layer also are the letters R and L (right and left). The board is completed by the addition of two layers of three-ply wood, one on each side of the center portion, all three being firmly glued together. On the top layer, two number guides are countersunk in such a manner that small lead numerals may be slipped into the guides to indicate the date and the patient's serial number.

British Medical Journal, London

2: 1187-1228 (Dec. 29) 1934

Estrus Producing Hormones. E. C. Dodds.—p. 1187.
Problem of the Septic Hand. R. Kennon.—p. 1189.
Tropical Sprue and Its Modern Treatment. N. H. Fairley.—p. 1192.
*Fatal Case of Subacute Yellow Atrophy of Liver After Cinchophen. T. N. Fraser.—p. 1195.
Advantages of Nitrous Oxide and Air Analgesia in Midwifery of General and Hospital Practice. J. Elam.—p. 1196.
Postoperative Management of Acute Empyema Thoracis. G. A. Mason.—p. 1197.

Fatal Case of Atrophy of Liver After Cinchophen.—Fraser cites a fatal case of acute rheumatism, which failed to respond properly to the usual remedies and was then treated with cinchophen. The total amount of cinchophen taken was 37½ grains (24.4 Gm.), at the rate of one tablet on five successive days. Jaundice appeared five days after the beginning of treatment. The question of idiosyncrasy has been raised by some authorities (Rabinowitz, Weir and Comfort) and probably had some connection in this case owing to the small dose of the drug that was taken. The pathologic features were quite classic and were similar to those of other reported cases; they were of interest from the close resemblance to the condition encountered in cases of trinitrotoluene poisoning. The advisability of the abandonment, or at least better control, of the administration of cinchophen should be considered.

1: 1-46 (Jan. 5) 1935

We Have Reason to Think. W. L. Brown.—p. 1.
Laboratory Testing of Disinfectants. L. P. Garrod.—p. 5.
Provision for Major Surgical Treatment of Pulmonary Tuberculosis. F. Heaf.—p. 8.
Review of One Hundred Consecutive Gallbladder Operations. J. M. Black.—p. 11.
Preventive Immunization in an Institutional Epidemic of Scarlet Fever. F. L. Scott and W. Morton.—p. 12.
So-Called Acidosis in Childhood: Note. R. A. M. Scott.—p. 13.

1: 47-92 (Jan. 12) 1935

The Surgeon and Pain. J. R. Learmonth.—p. 47.
Familial Acholuric Jaundice Simulating Lederer's Anemia. R. M. Murray-Lyon.—p. 50.
Preoperative Preparation of Cases with Grave Intra-Abdominal Hemorrhages: Note. K. H. Watkins.—p. 52.
Sarcoma of the Tongue: Report of Case. J. C. Ross.—p. 54.
*Treatment of Cholera with New Anticholera Serum: Preliminary Note. H. Ghosh.—p. 56.

Treatment of Cholera with Anticholera Serum.—Ghosh obtained by anaerobic culture of the cholera vibrio in a special broth a toxin which, when injected in small doses intravenously in rabbits, produced cholera-like diarrhea. He obtained sufficient corroborative evidence of the presence of a toxin in this medium by experimentally producing cholera-like diarrhea in laboratory animals. This toxin was prepared from only one strain of cholera vibrio, as it was found to produce uniform toxin, provided the medium was prepared exactly according to formula. The production of toxin depended on conservation of the virulence. The author observed clinically that a single sodium chloride transfusion and a single intraperitoneal injection of from 30 to 40 cc. of serum, according to the severity of the symptoms, diluted with 200 cc. of physiologic solution of sodium chloride diminished the frequency of the stool within two or three hours, and the patient usually passed urine within four to five hours. Of thirty-two cases treated during the second exacerbation of an epidemic, as evidenced from the increase in the rate of mortality in control cases, only four patients died, of whom one was admitted to the hospital three days after the onset of the disease, one died of excessive purging following administration, by mistake, of high doses of sodium phosphate, and the other two died within two hours of admission before the serum could be absorbed. Of 198 serum treated patients forty died, whereas seventy-three of 211 control patients died.

Clinical Science, London

1: 327-414 (Dec. 27) 1934

*Observations on Maladies in Which Blood Supply to Digits Ceases Intermittently or Permanently and on Bilateral Gangrene of Digits: Observations Relevant to So-Called "Raynaud's Disease." T. Lewis and G. W. Pickering.—p. 327.

Observations on Rate of Water Loss by Man at Rest: Part I. Description of Constant Temperature and Humidity Room: Part II. Spontaneous Diuresis During Prolonged Rest. P. D'Arcy Hart and E. B. Verney.—p. 367.

*Cerebrospinal Fluid Pressure in Arterial Hypertension. G. W. Pickering.—p 397.

So-Called Raynaud's Disease.—Lewis and Pickering point out that, if all instances of temporary arrest of the circulation to the finger or to any other part of the body that is particularly prone to become cold and all instances of symmetrical gangrene of digits without demonstrable obstruction to the main arteries of the limb are still to be classed as instances of "Raynaud's disease," a number of quite distinct conditions will continue to be grouped together. Such grouping cannot fail to obstruct inquiry into the causation of the various maladies and to prevent proper appreciation of their natural history. Many distinct maladies are being confused together and their separation is quite essential to the progress of future studies. The authors use the term "Raynaud's phenomenon" to signify active and intermittent closure of small arteries of the order of those supplying the digits, a closure manifesting itself clinically in a pallid or fully cyanotic state of the affected skin. This phenomenon can be a purely spasmodic affair; but it can come also when there is obstructive disease in the digital arteries themselves or in vessels proximal to these, this structural disease being ultimately responsible for the whole circulatory abnormality. The original disturbance may be a sudden and nonrecurring event, leaving behind it a proneness to attacks of cyanosis, which wrongly are regarded as signifying active disease. The events in each case must be regarded on their individual merits, and abnormal vasomotor influences should not be invoked in explanation because it has become the traditional and convenient line of reasoning for the whole group, but only when there is clear supporting evidence of such causation. It is a mistake to consider gangrene as the result of an uncomplicated spasmodic disorder. When the circulation to the skin is shut off, there comes into immediate action a mechanism producing vasodilatation and manifesting itself ultimately in "reactive hyperemia." Constriction of the vessels, produced through sympathetic channels, will counteract this dilator mechanism in the early stages of its establishment; but as ischemia is continued the vasodilator factor will become increasingly intense, and sooner or later the nerves themselves will become functionless locally. Thus it would seem inevitable that a nervous vasoconstriction cannot be maintained sufficiently long to kill the skin. When gangrene occurs, a structural change such as thrombosis has happened and permanently plugs the vessel. The view that thrombosis is an important factor must rest ultimately on microscopic demonstration, and microscopic examination of the tissues concerned has not yet been carried nearly far enough. The authors suggest that intimal changes including thrombosis are usually or always responsible for the obliteration of small arteries leading to necrosis, and they have in mind not only the isolated attacks of discoloration and necrosis such as are seen in the bilateral digital gangrene but also the minute necrotic foci which form on the fingers in cases that are primarily spasmodic.

Cerebrospinal Fluid Pressure in Arterial Hypertension.—Pickering states that the general clinical features presented by hypertensive patients with cerebrospinal fluid pressures of 250 mm. of water and more contrast strongly with those presented by patients having lower pressures. The former are younger, the kidneys are usually severely damaged and the disease progresses rapidly to a fatal termination. The latter are older, the kidneys usually escape severe damage and the disease progresses less rapidly. Every patient with a cerebrospinal fluid pressure of more than 250 mm. of water developed albuminuric retinitis. With one exception, every patient with a lower cerebrospinal fluid pressure had either no retinal lesion or the lesions characterizing arteriosclerotic retinitis. The author suggests that the essential difference between these two forms of retinitis is the addition in the albuminuric type of neuroretinal edema resulting from increased intracranial pressure. In individual patients with high blood pressure, the cerebrospinal fluid pressure has been found unaltered during headache and during acute attacks of coma and convulsions unassociated with uremia. There is a relation between high diastolic blood pressure and high cerebrospinal fluid pressure; and the former is one of the factors determining the latter.

Indian Journal of Medical Research, Calcutta

22: 199-424 (Oct.) 1934

Foundation of Biochemical Method of Standardizing Vitamin D or Irradiated Ergosterol. N. K. Basu.—p. 199.

Simple Method of Growing Hookworm Larvae. P. A. Maplestone.—p. 203.

Studies on Vitamin B_1: Part I. Solubility of Vitamin as Present in International Standard Preparation. G. Sankaran and N. K. De.—p. 215.

Id.: Part II. Iso-Electric Point as Determined by Electrophoresis of Solutions of Vitamin Made from International Standard Preparation. G. Sankaran and N. K. De.—p. 233.

Iodine Content of Indian Foodstuffs. M. Patnaik.—p. 249.

Some Common Indigenous Remedies. R. N. Chopra and S. Ghosh.—p. 263.

Biologic Assay of Digitalis Preparations in Tropics: Part IV. R. N. Chopra, J. S. Chowhan and N. De.—p. 271.

Id.: Part V. Potency of Lanadigin (Glucoside of D. Lanata) and Its Relation to Standard Digitalis Powder (B. P. 1932). R. N. Chopra, J. S. Chowhan and S. Lal.—p. 279.

Some Inorganic Preparations of Indian Indigenous Medicine: Part I. Abhra Bhasma. R. N. Chopra, S. Ghosh and A. Dutt.—p. 285.

Some Experimental Observations on Venom of Indian Cobra. K. Venkatachalam and A. N. Ratnagiriswaran.—p. 289.

Studies of Antigenic Structure of Vibrio Cholerae: Part VII. Two Acid Soluble Protein Fractions. R. W. Linton and B. N. Mitra.—p. 295.

Structure of Cholera and Cholera-like Vibrios: Notes. R. W. Linton, D. L. Shrivastava and B. N. Mitra.—p. 309.

Staining of Mycobacterium Leprae in Tissue Sections: Note. J. Lowe.—p. 313.

Bacteriophage, Essential Oils and Vaccination and Their Effects on Cholera Mortality. J. Morison, E. M. Rice and R. A. Haythornthwaite.—p. 317.

Studies on Nutritive Value of Milk and Milk Products: Part I. N. C. Datta and B. N. Banerjee.—p. 341.

Studies in Lipoid Metabolism: Part I. Variation in Cholesterol Content of Blood and of Different Organs in Pigeons Consequent on Administration of Chloroform. N. C. Datta.—p. 353.

Concentration of Antivenene by Ammonium Sulphate Method. S. D. S. Greval.—p. 365.

Nutritive Value of Indian Vegetable Foodstuffs: Part V. Nutritive Value of Ragi (Eleusine Coracana). S. P. Niyogi, N. Narayana and B. G. Desai.—p. 373.

*Relationship of Skin and Nerve Leprosy. E. Muir.—p. 383.

Cutaneous Leishmaniasis as Natural Infection of Dog in India. J. A. Sinton and H. E. Shortt.—p. 393.

Use of Bacteriophage Against Cholera in North Arcot District, Madras Presidency, in 1933. K. C. K. E. Raja.—p. 397.

Relationship of Skin and Nerve Leprosy.—Muir explains the distinction between neural and cutaneous leprosy by the aid of histologic observations and the leprolin test. The main factor determining the one type from the other is shown to be the degree of resistance. Another important factor is the relatively low resistance and cellular response to lepra bacilli in the subcutaneous nerves as compared with the skin. The importance is dwelt on of the distinction between resistant and nonresistant types in the diagnosis, prognosis, prevention and treatment of leprosy. For examining and comparing early lesions of the cutaneous and neural types, small elliptic pieces of skin and subcutaneous tissue with nerve branches attached are excised from typical macular lesions. Their similarity to the larger macules makes their nature recognizable, and as they are small the whole lesion can be excised. The main clinical distinctions between the neural and cutaneous macule are, in the neural macule, anesthesia on light touch, raised and indurated, marked erythema, marked keratosis, anhidrosis and depilation and recognizable hypopigmentation, especially if capillaries are emptied by pressure with a watch-glass; and, in the cutaneous macule, sensation on light touch, flat and soft, erythema slight or absent, keratosis, anhidrosis and depilation slight or absent and hypopigmentation generally more easily recognized. There is greater cellular response, in spite of fewer bacilli being present, in the neural than in the cutaneous type of macule. Especially in the cutaneous type there is, in proportion to the concentration of bacilli in the corium and nerves, far greater cellular response in the former than in the latter. The bacillary concentration is greater in the nerves than in the corium, this being most noticeable in the neural type.

Journal of Tropical Medicine and Hygiene, London

38: 1-16 (Jan. 1) 1935

*Clinical Study of Spleen in Blackwater Fever. A. D. Charters.—p. 1.
Experimental Transmission of Trypanosoma Rhodesiense Through Antelopes and Glossina Morsitans to Man. J. F. Corson.—p. 9.
Influence of Symbiosis on Pfeiffer's Bacillus. E. T. Thompson.—p. 11.

The Spleen in Blackwater Fever.—Charters gives a description of fifteen cases of blackwater fever showing the importance of splenic contraction in the causation of the disease, age incidence and period of residence in the endemic area, tendency to recurrence, prognosis, treatment and prophylaxis. Contraction of the spleen, which is often brought on by stimulation of the sympathetic nervous system, is an essential factor in the causation of blackwater fever. The predisposing effect of blackwater fever is seen only when the last attack has left an enlarged spleen. The prognosis depends on the degree and on the rapidity of contraction of the spleen. The tenderness of the enlarged spleen is an important pre-blackwater fever sign. Immunity is for the most part hereditary in character. Quinine is contraindicated during the hemoglobinuric stage but is a valuable adjunct to treatment when administered in graduated dosage twenty-four hours after the cessation of blackwater fever. Support is given to the theory that post-blackwater pyrexia is due to a persistence of the hemolytic process, relatively mild in degree. Quinine destroys parasites in the spleen by means of its property of causing splenic contraction, which results both in entrance of the drug into the pulp spaces and in expulsion of the plasmodia into the general circulation. In blackwater fever the acute dissolution of malarial parasites is brought about in the same way, the abundance of antitoxin rendering this possible in those cases of the disease which are not preceded by a dose of quinine. A suggested method of treatment is the arrest of splenic contraction by means of splanchnic anesthesia. Prophylaxis depends on regular abdominal examination and on a course of quinine to any patient who shows enlargement of the spleen. When this organ becomes impalpable, administration of the drug is no longer necessary.

Lancet, London

1: 1-68 (Jan. 5) 1935

Differential Diagnosis of Pregnancy. A. L. Robinson and M. M. Datnow.—p. 1.
*Cerebral Vascular Accidents Unassociated with Cardiovascular Disease. J. St. C. Elkington.—p. 6.
*Saccular Aneurysm of Thoracic Aorta Treated by Wiring with Colt's Apparatus. T. Thompson, H. S. Souttar and L. Howells.—p. 11.
Agranulocytosis Due to Amidopyrine: Experimental and Clinical Study of Seven New Cases. P. Blum.—p. 14.
Digestibility of Common Foodstuffs as Determined by Radiography. W. C. D. Maile and K. J. L. Scott.—p. 21.

Cerebral Accidents Unassociated with Cardiovascular Disease.—Elkington draws attention to the occurrence of cerebral vascular accidents in healthy persons without cardiovascular disease, describing four cases that are believed to be of this nature. In none of them were the usual causes of cerebral embolism, thrombosis or hemorrhage present. The sudden onset was suggestive of hemorrhage. In two cases the attacks occurred under circumstances in which it might be supposed that the systolic blood pressure was higher than usual. In the absence of any evidence of cardiovascular disease it seems probable that the vascular disturbance had occurred in or round some preexisting local abnormality. The physical signs in each case suggested a well defined intracerebral lesion. In three cases the combination of aphasia, homonymous field defects involving central vision and transitory sensory disturbance pointed to lesions of the left temporal lobe, while in the other case the signs suggested a destructive lesion in the right cerebellar hemisphere. Although the cerebrospinal fluid was not examined immediately after the attack, no freshly shed blood was found. In two cases the faintly yellow discoloration of the fluid was explained as due to a previous subarachnoid hemorrhage or to an intracerebral hemorrhage at some distance from the ventricle or subarachnoid space. These features make it unlikely that these cases were due to the leakage of cerebral aneurysms. The benign course of the cases makes it improbable that they were due to gliomas, especially as those growths which undergo sudden degenerative change are usually of a rapidly progressive order. A more probable explanation of the nature of these lesions is suggested by the pathologic observations in a similar case, which show that a hemorrhage had occurred into the substance of a preexisting vascular abnormality of the left half of the pons and left middle cerebellar peduncle. This abnormality had the features of a telangiectasis and was not associated with any vascular abnormality elsewhere in the nervous system or in the skin or other organs. Reference to the literature shows that it is not only capillary telangiectases which are liable to give rise to intracerebral hemorrhage in apparently healthy persons, as similar vascular accidents may occur in association with malformations composed of larger vessels—i. e., arteriovenous angiomas. Unlike the capillary telangiectases that are common in the contents of the posterior fossa, the arteriovenous anomalies appear to have a preference for the posterior part of the cerebral hemispheres. The favorable outcome in the author's four cases causes him to speculate on their pathology. However, their close clinical resemblance to other cases in which postmortem examination has been carried out makes it probable that they were caused by hemorrhage into a vascular anomaly of the type of a telangiectasis or an arteriovenous angioma.

Saccular Aneurysm of Thoracic Aorta.—Thompson and his associates present a case of saccular aneurysm of the thoracic aorta in which Colt's method of introducing an expanding wire umbrella has proved successful. The patient received a series of blows on the chest directly before the symptoms of aneurysm appeared. In spite of rest and antisyphilitic treatment the aneurysm was increasing in size, protruding between the ribs and reddening the skin, so that rupture seemed an imminent probability. When Colt's umbrella of gold wire was inserted the tumor sank back into the chest and the severe pain was relieved. Since that time regular inspections of the chest have been made and the improvement has continued over a period of three and a half years after the operation. At the last observation the patient was almost free from symptoms and examination of the chest merely showed a slight pulsation over the seat of the aneurysm. The presence of a positive Wassermann reaction showed clearly that the underlying basis was syphilitic, but the onset of symptoms within a few days of receiving severe blows on the chest would point to the trauma being a predisposing cause. The author believes that the indications for the use of Colt's gold wire wisps in cases of thoracic aneurysm appear to be: 1. Definitely saccular aneurysm and not a mere general dilatation of the aorta. 2. Failure of a previous course of rest and antisyphilitic treatment to prevent an increase in the size of the aneurysm. 3. Involvement of the chest wall and reddening of the skin, suggesting imminent rupture of the sac. 4. Evidence of pressure on the esophagus or left bronchus, especially if small quantities of blood have been expectorated.

Medical Journal of Australia, Sydney

2: 831-860 (Dec. 29) 1934

March of Cardiology. E. Russell.—p. 831.
Chronic Alcoholism: Being Experiences and Conclusions of a General Practitioner After Nearly Fourteen Years of Addiction, with Recovery. An Anonymous Contributor.—p. 840.
Surgical Treatment of Chronic Duodenal Ulcer. H. C. Rutherford-Darling.—p. 843.

1: 1-36 (Jan. 5) 1935

An Address. W. N. Robertson.—p. 1.
Concerning Rôle of Heredity in Diabetes Mellitus: I. Incidence and Character of Hereditary Diabetes. K. Maddox and Madeleine Scott.—p. 7.
Sinusitis in Children. C. Cantor.—p. 13.

Chinese Medical Journal, Peiping

48: 1181-1338 (Dec.) 1934

Observations on Maturation of Erythrocytes in Albino Rat. W. C. Ma.—p. 1194.
Craniocerebral Survey of Australian Aboriginal. J. L. Shellshear.—p. 1202.
Development of the Upper Eyelid of Chinese, with Especial Reference to the Mongolian Fold. I. C. Wen.—p. 1216.
Anthropologic and Roentgenologic Observations on Pelves of Chinese Women. H. E. Scheyer.—p. 1228.
Cutaneous Nerves of the Chinese Foot. M. T. P'an.—p. 1235.
Coronary Arteries of the Chinese Heart. M. T. P'an.—p. 1247.
Measurements and Observations on Certain Aboriginal Tribes of Szech'Uan Province. W. R. Morse and A. Yoh.—p. 1267.
Some Observations on Northern Chinese Skulls. C. Chang.—p. 1282.
Anthropometric Study of Students of Chosen Christian College. R. K. Smith.—p. 1289.
Interrelation of Biometric and Clinical Methods in Appraisal of Nutritional Status. P. H. Stevenson.—p. 1295.
Plea for Continuation of Cooperative Embryologic Research in China. P. H. Stevenson.—p. 1313.

Annales de Médecine, Paris

37: 1-144 (Jan.) 1935

Bronze Diabetes (Pigmentary Cirrhosis of Liver and Diabetes). M. Labbé, R. Boulin and M. Petresco.—p. 5.
Study of Hepatic Amylosis. M. Labbé, R. Boulin, I. Bertrand and L. Justin-Besançon.—p. 40.
Icterogenic Spirochetosis of Catarrhal Jaundice Form. M. Brulé.—p. 62.
*Purpura in Hepatic Disease. P. Abrami.—p. 71.
*Test of Galactosuria and Diagnosis of Hepatic Insufficiency. M. Labbé and F. Nepveux.—p. 80.
Physicochemical Factors in Formation of Gallstones. V. de Lavergne and P. Kissel.—p. 105.
Critical Study of Pathogenic Theories of Biliary Lithiasis. V. de Lavergne and P. Kissel.—p. 117.
Therapeutic Agents of Biliary Secretion. E. Chabrol and R. Charonnat. —p. 131.

Purpura in Hepatic Disease.—Abrami analyzes the purpura occurring in hepatic disease with a view to deciding whether this is a separate entity. The purpura of hepatic disease presents, he says, all the characters of hematogenic purpura. The question, then, is whether hepatic changes alone can produce spontaneous capillary ruptures, lengthening of the bleeding time, decrease of platelets and nonretraction of the clot. He concludes that the only one which can be undeniably assigned to the liver is deficiency of blood coagulability. He therefore believes that this group of purpuras belongs with those of hematogenic type and that the changes of the liver are wholly unable to produce the stigmas of hematogenic purpura. The existence of a separate hepatic purpura should thus be abandoned.

Galactosuria and Hepatic Insufficiency.—Labbé and Nepveux examined the value of the galactose test of liver function in normal and diseased persons. Simultaneous examinations of galactosuria and glycemia were made. The subjects were given 40 Gm. of galactose dissolved in 200 cc. of water before breakfast. The glycemia was measured before breakfast and every following half hour. At the same time urine was collected and analyzed for galactose. If the galactosuria was not ended after three hours, collection was continued during the day to obtain the total twenty-four hour galactose excretion. The same method was followed on another day after ingestion of 50 Gm. of dextrose. Seven healthy medical students furnished the normal subjects. The test was also carried out on nine patients with alcoholic cirrhosis, two with hypertrophic cirrhosis and diabetes, one with cardiac cirrhosis, two with catarrhal jaundice, one with chronic icterus and lithiasis, and five other patients. The results, tabulated in detail, were interesting but not superior to the usual dextrose test. If galactosuria is produced more easily than glycosuria, it does not mean a greater difficulty for the liver in fixing galactose or an incapacity of the tissues to use this sugar but simply that the permeability of the kidneys is greater for galactose than for dextrose. Hence there seems to be no valid reason for substituting galactose for dextrose in the functional examination of the liver. The authors also point out that the galactose test must be considered only a test of the glycogenic function of the liver and not an index of general hepatic function, since it is well known that liver functions are multiple and relatively independent of one another.

Presse Médicale, Paris

43: 97-120 (Jan. 19) 1935

*Cancer of Stomach in Cured Pernicious Anemia. P.-É. Weil and J. Bernard.—p. 97.
*Symptomatologic Value of Arterial Hypertension in Cranial Traumatisms. P. Wertheimer and P. Frieh.—p. 99.
Intercostal Neurolysis in Treatment of Pulmonary Tuberculosis According to Leotta Method. F. Rabboni.—p. 102.

Cancer of Stomach in Pernicious Anemia.—Weil and Bernard describe the case of a man with pernicious anemia treated successfully for eight years. Finally death occurred following a short period of aggravated symptoms. Necropsy revealed a typical gastric epithelioma on the large curvature of the stomach, with extensive infiltrations. The authors believe that such experiences may become more frequent now that patients with pernicious anemia are usually granted a longer period of life. Two possible explanations are suggested: anatomic and functional. It is well known that cancers develop on chronic inflammatory lesions and it is suggested that the gastric aplasia noted in pernicious anemia may serve in this rôle. The functional interpretation is based on the possible dissociation of hematopoietic and digestive function in pernicious anemia. Thus the cases of cancer coexisting with or evolving after anemia may be interpreted in an identical manner.

Hypertension in Cranial Traumatisms.—Wertheimer and Frieh believe that the blood pressure should be recorded four times a day after cranial traumatisms. The absence of arterial hypertension excludes the presence of a block. The retention of normal arterial tension does not, however, insure a favorable prognosis. The prognosis depends on the clinical signs and their development, such as variations of the cerebrospinal fluid pressure. Elevation of the arterial pressure, especially if rapid, associated with a constantly low cerebrospinal fluid pressure indicates the presence of blockage. In cases in which careful lumbar puncture, with drop by drop removal of fluid, lowers the level of arterial tension the diagnosis of "relative" blockage is indicated; if under the same conditions the arterial tension remains the same, the blockage is complete. On this basis it seems that therapeutic measures may be more accurately applied.

Policlinico, Rome

42: 65-128 (Feb. 1) 1935. Medical Section

Variations of Hydroprotein Constitution of Blood Between Artery and Vein. P. Stefanutti.—p. 65.
*Hypophonesis on External End of Clavicle According to Pende to Indicate Incipient Apical Changes. F. L. Cassone.—p. 78.
Primary Pulmonary Carcinoma. G. Becchini.—p. 89.
*Alkali Reserve in Hypoglycemia in Normal Persons and Diabetic Patients. M. Tripodi.—p. 111.

Hypophonesis on External End of Clavicle.—Cassone states that the pulmonary apex frequently becomes the seat of the first productive lesions of tuberculosis. He reviews the symptomatology of a patient presenting specific lesions and in whom palpation, percussion, auscultation and roentgen examination of the apical regions were made. He discusses the value of each of these signs and their possible causes of error. Percussion was done on the external end of the clavicle, according to Pende, in patients having presented apical lesions in previous examinations and in patients in whom a diagnosis of a specific initial form was made from ectoscopic and anamnestic symptoms. The author found that in the first group of patients percussion indicated dulness in a clearer and more precise manner than when percussion was done on the apical region. In the second group, percussion indicated immediately the localization of the disease and showed apical involvement. This was confirmed in many patients by a roentgenogram showing opacity and small dark circumscribed spots of the apex, and also by auscultation revealing fine and fixed râles. Having observed that the dulness on the external end of the clavicle is present when there are no trophic changes of the muscles of the shoulder and even when the signs of apical catarrh are lacking, the author concludes that it is one of the early appreciable pulmonary signs of apical lesions and is of marked symptomatologic value for the diagnosis of incipient tuberculosis.

Alkali Reserve in Hypoglycemia.—Tripodi studied the behavior of the alkali reserve during the course of hypoglycemia artificially induced by subcutaneous injections of insulin in normal persons and diabetic patients. He found that the postinsulin glycemic depression is constantly accompanied by a decline in the alkali reserve of normal persons and patients presenting mild nonacidotic diabetes. This decline coincides with the appearance of hypoglycemic symptoms and is proportionate to their gravity. In grave acidotic diabetes there is an increase in the alkali reserve in the first stage and, when in the second stage the glycemic rate falls below a certain limit, variable in diabetic patients, there is a decline in the alkali reserve. Contrary to what was observed in normal persons and in patients with mild diabetes, the appearance of the first hypoglycemic symptoms does not coincide with a diminution of the alkali reserve but with an increase in it. If the hypoglycemic symptoms become more serious, the alkali reserve is lowered, but not always to the level preceding the administration of insulin. The author injected large doses of sodium bicarbonate intravenously in normal persons and in diabetic patients during hypoglycemic symptoms. This injection exerts a favorable action on mild hypoglycemic symptoms, such as

perspiration, tremors, nervousness and rapid pulse. It does not arrest their evolution or improve the more serious hypoglycemic manifestations, such as debility, somnolence, convulsions and coma.

Dermatologische Zeitschrift, Berlin

70: 249-308 (Jan.) 1935. Partial Index

Glandular and Exfoliative Cheilitis. A. Jordan and A. Tarabuchin.—p. 249.
*Complement Fixation in Fungus Diseases. F. Földvári.—p. 260.
Advantages of Buffer Action in Treatment of Eczema. A. Papendieck.—p. 269.
*Multiple Fibromatosis of Skin After Frost Bite. D. A. Zipersson.—p. 279.

Complement Fixation in Fungus Diseases.—Földvári used in his studies of complement fixation in fungus diseases two antigens: (1) a polyvalent antigen prepared from Achorion Quinckeanum, Achorion Schoenleinii and various strains of Trichophyton and of Epidermophyton, and (2) an antigen prepared from strains of Trichophyton gypseum. He concludes that antibodies producing complement fixation are produced in considerable quantities in the deep seated fungus diseases. In the more superficial processes, the antibodies are formed in smaller quantities. Vaccine therapy promoted antibody formation in some of the cases, while in others it exerted no influence on the antibodies. The complement fixation test was of no value for the prognosis. The vaccine had the same therapeutic effect, whether the antibodies were increased or not. The allergic reactions did not always run parallel with the complement fixation reactions. It appears that the reactions are group reactions. The deviation of the complement seems to be of diagnostic value in fungus diseases with deeper processes (blastomycosis, sporotrichosis) or with eczematous or dyshidrotic changes in which the microscopic or cultural demonstration fails.

Multiple Fibromatosis of Skin After Frost Bite.—Zipersson describes the case of a woman, aged 30, who had approximately 800 nodules and tumors. She stated that the disorder began at the age of 2, after she had been exposed for a long period to the cold of winter. The histologic examination of two growths corroborated the diagnosis of multiple fibromatosis of the skin. The author mentions other writers who have observed cases of fibromatosis of the skin after exposure to cold. The multiplicity is especially characteristic for these fibromas. The growths are distributed over the entire body. The mechanism of development of the fibromas is not completely understood, but several theories have been suggested. The prognosis is rather unfavorable, since there is danger of malignant degeneration, necrosis and calcification. Treatment is generally of little avail, but, if the fibromas become large, surgical intervention is advisable.

Deutsches Archiv für klinische Medizin, Berlin

177: 97-208 (Dec. 28) 1934. Partial Index

Clinical Report of Case of Transitory Heart Block with Abnormal Frequency of Ventricle. L. Delius.—p. 107.
Alkali Therapy of Supersecretion and Superacidity. K. P. Becker.—p. 115.
*Clinical Examination of Carbohydrate Metabolism with Consideration of Its Modification by Creatine. D. Jahn.—p. 121.
Blood Pressure Increasing Substance in Cerebrospinal Fluid, Particularly During Hypertension. E. Kylin, T. Kjellin and H. Kristensson.—p. 139.
*Course of Galvanic Skin Reflex in Sympathetic Neuroses. K. W. Essen.—p. 144.

Carbohydrate Metabolism and Its Modification by Creatine.—Jahn shows that it is necessary to determine, in addition to the blood sugar curve after the dextrose tolerance test, the fluctuations in the lactic acid content and in the ketonic acid content so as to obtain information about the site of the utilization of sugar. Dextrose tolerance tests with and without physical exertion reveal the great differences in the rapidity of the utilization of sugar during rest and during physical exertion. Observations make it probable that substances from the muscular metabolism play a part in the regulation of the utilization of sugar. Studies on the metabolic action of creatine reveal a tendency to limitation of combustion of sugar in the tissues. In case of glycogen deficiency in the liver, there develops after the application of creatine a considerable ketonemia and a reduction in the blood sugar content. However, the reduction in the lactic acid content of the blood is observable in all cases. Creatine promotes the insulin action on the glycogen formation in the muscles and supports the blood sugar reducing action of the hormone. The contradictory changes in the lactic acid and in the ketone body contents of the blood can be explained by the action of the muscular substances that increase the insulin action. If clinical examination reveals a disturbance in the carbohydrate metabolism with hypoglycemia and ketonemia, the disturbance should be brought into relation with the reduction of the blood sugar after muscular exertion and carbohydrate intake and with the aspects of spontaneous hypoglycemia.

Galvanic Skin Reflex in Sympathetic Neuroses.—Essen points out that the sympathetic apparatus of persons with a sympathetic neurosis has a deficient compensation capacity. He demonstrated this in the galvanic skin reflex that develops after a short cough. He tested this reflex in forty-six healthy persons and eighty-two persons with a sympathetic neurosis. Of the forty-six healthy persons, forty showed normal reflex action, and of the eighty-two with sympathetic neurosis, sixty-three showed a pathologic reflex. The abnormal reflex action was indicated by a prolongation of the latent time and of the time of disappearance and by fatigability and an undulated outline of the reflex record. The author concludes that the abnormal galvanic skin reflex is a frequent and significant sign of sympathetic neuroses. The galvanic skin reflex exemplifies that the dynamic course of sympathetic regulations is abnormal in persons with sympathetic neurosis.

Klinische Wochenschrift, Berlin

14: 113-144 (Jan. 26) 1935. Partial Index

Concentric Hypertrophy of Heart and Toxogenic Hypertension. J. Pal.—p. 116.
Follicular and Corpus Luteum Hormones in Their Reaction on Anterior Lobe of Hypophysis. C. Clauberg and W. Breipohl.—p. 119.
*Clinical Significance of Green Fluorescence in Blood Serum. W. Brunner.—p. 121.
*Primary Point of Attack of Allergens as Foundation of Allergic Tests and Therapy. E. Urbach.—p. 124.
Tumor Immunity. Z. Zakrzewski and H. J. Fuchs.—p. 127.

Green Fluorescence in Blood Serum.—To determine the degree of urobilinemia in disorders of the liver or the kidney, Brunner employed his method for the quantitative determination of the maximal green fluorescence in the blood serum. He devised this method because Heilmeyer's quantitative determination of urobilinogen proved satisfactory only for the examination of feces and urine but not for the blood serum. To 1 cc. of blood serum the author adds 0.5 Gm. of pulverized zinc acetate, mixes well and lets it stand for twelve hours at room temperature. Then he adds 7 cc. of absolute alcohol and shakes well. This mixture has to stand for twelve hours and then is filtered into test tubes. The absolutely clear filtrate is examined colorimetrically in the arc light simultaneously with a series of dilutions of ethoxy-diamino-acridine-lactate (from 1:200,000,000 to 1:10,000,000). To obtain a clearer picture of the quantities of urobilin, the values were changed by computation into milligrams per hundred cubic centimeters. The normal urobilin content of the blood serum is estimated at between 0.0628 and 0.125 mg. per hundred cubic centimeters of blood serum, which corresponds to a solution of ethoxy-diamino-acridine-lactate of from 1:200,000,000 to 1:100,000,000. The author found that the determination of the urobilinemia is a more reliable and exact indicator for the disordered hepatic function than is urobilinuria. This could be observed particularly in insufficiency of the kidneys. In icterus that is caused by complete occlusion and in catarrhal icterus there exists in spite of fecal acholia and of usually greatly reduced urobilinuria a severe urobilinemia (autochthonous formation of urobilin in the liver). In chronic, true uremia uncomplicated by cardiac insufficiency and cirrhosis of the liver, the urobilinuria remains within normal limits. This indicates that the liver is not involved in the development of true uremia. The author thinks that the anemias accompanying uremia are probably not the result of increased hemolysis but rather of the toxic insufficiency of the bone marrow.

Primary Point of Attack of Allergens as Foundation of Allergic Tests and Therapy.—Urbach states that the foundation of every clinical manifestation of an allergic dis-

order is an antigen-antibody reaction. In the individual case, the manifestation of the allergy is dependent less on the antigen but almost entirely on the localization of the cellular antibodies. The author reproduces a table in which the allergic diseases and the principal point of attack of the allergens are put in opposite columns. Classification of the allergies on the basis of the site of the antigen-antibody reaction explains why only a test that is performed on the shock organ can give information about the type and degree of allergization of the involved tissue. Moreover, it makes a more effective therapy possible, for only such desensitization is effective that considers the primary point of attack (epidermal, vasculocutaneous, vasculocerebral, epimucobronchial, leiomyobronchial and so on) and that is applied to the involved organ (epidermis, cutaneous vessels, bronchial mucous membrane, bronchial musculature and so on). If a few exceptions are disregarded, the clinical manifestations of an allergy are almost entirely determined by the organ in which the antigen-antibody reaction takes place. Allergic eczema was one of the conditions in which the primary site of the cellular antibodies was disputed. Whereas Kyrle considered the epithelial hypersensitivity the only basis of eczematous manifestations, Jadassohn and his collaborators came to the conclusion that a purely epithelial hypersensitivity without the involvement of the cutaneous vascular system is not likely and assumed a vasculo-epithelial allergic origin. The author thinks that in eczema the primary site of the antibodies may be epithelial as well as vascular. Recent histologic studies indicate that the reticulohistiocytic elements of the epidermis (the so-called Langerhans cells) and those of the cutis (the capillary endothelials of the papillary blood and lymph vessels) form a connected system, the so-called endothelial-Langerhans system. This would explain how a primary epidermal hypersensitivity later becomes elicitable by way of the vascular system. The differentiation of primary epithelial from primary vascular eczemas is done by epinephrine-iontophoresis. Just as in the skin, a differentiation is possible also in case of the mucous membranes (primary epimucous and primary vascular).

Medizinische Klinik, Berlin

31: 69-100 (Jan. 18) 1935. Partial Index

Diagnosis and Therapy of Hemorrhoidal Disturbances. A. W. Fischer.—p. 69.
*Hemolytic Anemia—Spherocytic Disease. H. Lehndorff.—p. 74.
Pathogenesis of Intestinal Occlusion by Meckel's Diverticulum. H. Steindl.—p. 77.
*Further Observations on Prophylactic Vaccinotherapy of Whooping Cough. W. Kaupe.—p. 79.
Sporadic Pellagra in Vienna and Lower Austria. J. Urbach.—p. 79.
Foreign Body in Retropharynx with Peripheral Relaxation of Larynx. H. Krsek.—p. 83.

Hemolytic Anemia—Spherocytic Disease.—Lehndorff shows that there are two types of hemolytic anemias, the idiopathic and the symptomatic forms. The latter type is usually caused by chemical or bacterial toxins, while the first type is endogenic, a congenital "hematic diathesis." The diathesis may remain latent for a long time, but its manifestation may be brought on by various factors, such as infections, exposure or overexertion. When fully developed, the disease presents three characteristic symptoms: icterus, anemic pallor and splenic tumor combined with three hematologic signs: microcytosis, reduced resistance of the erythrocytes to hypotonic solution of sodium chloride and increase of reticulocytes. However, these symptoms need not all be present at the same time. In children the icterus is almost never severe and in some instances it is entirely absent. There are also cases without splenic tumor and some without pallor. The most characteristic signs of the disease are found on examination of the blood. The most important symptom is the microcytosis. The diameter of the erythrocytes is only 5.8 microns instead of 7.8 microns as in normal persons. Moreover, these are not the small erythrocytes, the micropoikilocytes, found in most forms of anemia. Instead of being disk shaped they are spherical, and in spite of their smaller diameter they have a greater volume than the normal erythrocytes (100 cubic microns instead of 88). For this reason the author thinks that for this type of cells the term spherocytes is better than the term microcytes. The hemoglobin content of the spherocytes is comparatively high, which explains the relatively high color index of 1 or higher in this type of anemia. Because the disk-shaped erythrocytes are the only suitable ones, it may be assumed that the organism tries to eliminate the spherical types by an increased activity of the reticulo-endothelial system, particularly the spleen. This results in splenic tumor. Icterus develops if the liver is no longer capable of utilizing the excessive amounts of pigment. The author thinks that the nature of hemolytic anemia is explained best by assuming a congenital abnormality of the erythropoietic system, as the result of which it produces spherical instead of disk-shaped erythrocytes. To support further the opinion that the spherical form of the erythrocytes is the essential factor in hemolytic anemia, he mentions other hemolytic conditions that are characterized by erythrocytes of abnormal shape. He calls attention to sickle-cell anemia and to erythroblastic anemia. He compares the main aspects of these two types with the described type and shows that the different types are characteristic for different races, the sickle-cell anemia, for instance, for the Negro race. In regard to the therapy of hemolytic anemia, he states that treatment is unnecessary during the latent stage and that blood transfusion is advisable during the acute attack. Occasionally, treatment with liver and iron may be helpful. Splenectomy should be done only in case of repeated hemolytic crises.

Prophylactic Vaccine for Whooping Cough.—Kaupe reports his experiences with whooping cough vaccine in a home for nurslings and an orphans' home connected with it. In the nurslings and children who had whooping cough, the vaccinotherapy resulted in a prompt cure. All other children were given three prophylactic injections of vaccine and, although they had been in contact with the children who had whooping cough, they remained free from it. The author emphasizes that all the children, even the infants of from 1 to 6 months, tolerated the vaccine well. The only symptom produced by the injections was a slight temporary increase in the temperature.

31: 101-132 (Jan. 25) 1935. Partial Index

Azotemias. W. Nonnenbruch.—p. 101.
Cardialgias and Aortalgias (Angina Pectoris). R. Schmidt.—p. 105.
Edematous Form of Herpes. R. Bezecny.—p. 109.
*New Treatment of Congenital Dislocation of Hip Joint by Means of Straddle Bandage. F. Bauer.—p. 110.

Treatment of Congenital Dislocation of Hip Joint.—Bauer says that the treatment of congenital dislocation of the hip joint with nonsurgical reduction and prolonged subsequent fixation had two aims: the correction of the abnormal position of the joint and the permanent retention of the head in the acetabulum. He devised a method which, in addition to these two aims has a third, the stimulation of the joint. He tries to accomplish this by excluding fixation from the treatment, because he considers it harmful for two reasons: It inhibits the joint stimulating action and produces atrophy of all parts of the joint. The new feature of his method is the straddle bandage. Reduction is done immediately after the condition has been recognized. It can be done during the first few weeks of life. Then the straddle bandage is adjusted. It can be made of rep ribbon from 2.5 to 3 cm. in width. A girdle that can be buttoned in front is placed round the thorax, and two shoulder straps secure the girdle against downward pull. Well fitting slings grasp both legs below the knee, and two pieces of ribbon of the proper length to secure correct abduction connect the slings of the legs with the girdle in the back. In case of slight abduction they are usually fastened on the same side, while in case of greater abduction they are fastened crosswise, on opposite sides. In older children, ribbons may be fastened also on the front of the girdle and connected with the slings round the legs. To secure continuous maximal abduction, a rod with holes at both ends may be fastened on the slings. Even if this is done there is still considerable freedom of movement. The bandage can be changed and washed. It is advisable to keep the bandage on during the daily bath. The author employed this bandage successfully in fourteen cases of congenital subluxation and in six cases of congenital dislocation. The treatment produces the best results if employed during the first year of life.

Monatsschrift f. Geburtshülfe u. Gynäkologie, Berlin

98: 257-320 (Jan.) 1935. Partial Index

Antithyroid Resistance of Various Types of Blood in Biologic Experiment. H. Eufinger and J. B. Gottlieb.—p. 257.
*Microsedimentation of Erythrocytes in Six Stages and Its Use in Gynecology and Obstetrics. F. Heimann.—p. 266.
*Sterility and Myoma of Uterus. M. Randazzo.—p. 270.
Frigidity in Women and Its Treatment. W. T. Schmidt.—p. 279.

Microsedimentation of Erythrocytes in Six Stages.—Heimann directs attention to the fact that careful observation of the course of sedimentation of the erythrocytes reveals that sedimentation does not take place evenly. Sometimes the column of erythrocytes decreases rapidly during the first few minutes and later descends more slowly, while in other instances sedimentation is retarded during the first few minutes and becomes more rapid later on. The six-phasic microsedimentation, in which a reading of the sedimentation is taken every fifteen minutes, is based on this observation. A specimen of blood is withdrawn and placed in a test tube with a diameter of 1 mm. and a 100 mm. scale, the blood reaching to the upper (zero) graduation mark. The readings are recorded and a curve is plotted. The test was made in 149 cases (200 sedimentations). The Linzenmeyer macromethod served as a control. In order to obtain a standard curve, the microsedimentation was first made on ten women, who appeared healthy. The curves obtained in these cases showed a rather even ascent up to the fifth phase, but in the sixth phase they again receded to the height of the fourth phase. Aside from slight individual differences the curves obtained in the ten healthy women were essentially the same, so that it is justifiable to compute from them a standard curve, characterized by a single peak that appears in the fifth phase and by an apical angle of about 135 degrees. The total sedimentation as a rule does not exceed 14 or 15 mm. The six-phasic microsedimentation aims at an analysis of the total complex of erythrocytic sedimentation. The separation of the complex into its components is possible, but only the apical deviation and the total sedimentation can be utilized independently. The total sedimentation corresponds to that in the macromethod. The apical deviation, which is a sensitive indicator of incipient changes in the colloidal structure of the blood, represents the chief advantage of the micromethod over the macromethod. However, this advantage is of practical significance only in the borderline cases. Because of difficulties in the technic, the author does not recommend the six-phasic micromethod for general use but only for certain borderline cases.

Sterility and Myoma of Uterus.—Randazzo shows that, although facts indicate that sterility may be caused by uterine myomas, conditions are more often reversed; that is, myomas develop in women who did not bear children.

Münchener medizinische Wochenschrift, Munich

82: 123-162 (Jan. 24) 1935. Partial Index

Action of Therapeutic Diphtheria Serum. U. Grüninger.—p. 125.
Traumatic Injury of Cervical Portion of Vertebral Column and Its Late Results. H. Baumecker.—p. 127.
Case of Isolated Injury of Cardiac Excitation Conducting System. W. Kampmann.—p. 129.
*After-Treatment of Patients Who Have Undergone Gastric Resection on Account of Ulcer. Graumann.—p. 132.
*Autohemotherapy in Puerperal Mastitis. L. Sinn.—p. 133.
Clinical Aspects of Tuberculosis of Palatine Tonsil. H. Willige.—p. 137.
Diagnosis of Carcinoma of Esophagus. P. Preuschoff.—p. 142.
*Studies on Blood with Infra-Red Photography. A. Fröhlich and G. Rodenacker.—p. 146.

Gastric Resection on Account of Ulcer.—Graumann discusses disturbances that develop after gastric resection following the first postoperative intake of food or previous to it. In their nature and changing intensity, these disturbances do not greatly differ from the typical ulcer symptoms. The patients complain particularly of eructation, of a feeling of pressure and occasionally also of vomiting and of pain while the stomach is empty. Ulcer is usually accompanied by gastritis and the symptoms of this gastritis persist into the postoperative stage. Moreover, the gastric mucous membrane responds with inflammation to the irritation produced by clamps, knife and sutures. This explains the considerable hypersecretion and the tendency to increased acidity. He tried to counteract the postoperative disturbances not only by the usual dietary measures but also by the oral administration of a glutinous calcium silicate, which, in the acid gastric juice, is split into silicic acid gelatin and calcium chloride and sodium chloride. This substance effected a rapid disappearance of the heartburn and acid eructations. In patients who had attacks of vomiting the effect was not quite so rapid, but they too were influenced favorably. After the first attack of vomiting the calcium silicate preparation was administered before each meal and, after two days at the latest, the disturbances disappeared. It is difficult to decide whether the preparation exerts a favorable effect on the bleeding, for blood transfusion and gelatin, which had proved successful in other cases, were not neglected here. Nevertheless, the author thinks that the preparation increases the calcium content of the blood and gives mechanical protection to the mucous membrane. Recently he has instituted this medication in all cases in which gastric resection has been done. As a result, the disturbances have become less frequent.

Autohemotherapy in Puerperal Mastitis.—Sinn states that in the last eighteen months this treatment was employed in sixty cases of mastitis. Blood is withdrawn from the cubital vein and immediately injected into the gluteal muscle. In acute cases 20 cc. is the usual quantity and the injection may be repeated after twelve and twenty-four hours under certain conditions. However, the third injection is hardly ever necessary. In subacute conditions from 3 to 5 cc. of blood is sufficient. The author did not have occasion to employ the method in chronic cases of mastitis, but he thinks that the injection will produce an increase of the processes of inflammation and thus accelerate healing. He points out that autohemotherapy, together with tying up of the breast and the application of icebags, is of especial value when roentgen rays and short waves are not available.

Studies on Blood with Infra-Red Photography.—Fröhlich and Rodenacker show that by means of infra-red photography it is possible to recognize carbon monoxide blood. With suitable wavelengths they were able to differentiate oxyhemoglobin from reduced hemoglobin. Moreover, they proved with infra-red photography the impairment of hemoglobin following complete dissociation of carbon monoxide hemoglobin, and they were able to give photographic proof of the favorable action of methylene blue in the clinical treatment of carbon monoxide poisoning. The authors are now conducting experiments to improve the method further and extend it to isolated hemoglobins.

Zeitschrift für urologische Chirurgie, Berlin

40: 211-368 (Jan. 10) 1935. Partial Index

*Experimental Studies on Development of Urinary Calculi. T. Hryntschak.—p. 211.
*Rôle of Sodium Chloride in Metabolism During Urologic Disturbances Particularly in Hypertrophy of Prostate. L. Strauss.—p. 242.
Foreign Bodies in Bladder. J. Minder.—p. 259.
Value of Vasectomy in Inflammatory Diseases of Epididymis. J. Minder. p. 266.
Pathogenesis of Urogenital Tuberculosis in Light of New Experimental Research. G. S. Epstein.—p. 276.

Experimental Studies on Development of Urinary Calculi.—Hryntschak succeeded in producing renal gravel in 80 per cent of the rabbits, in which he produced a moderate stasis in one kidney and then introduced intravenously Staphylococcus albus. In a few animals small concrements were found. Analogous experiments with colon bacilli, with Bacillus lactis-aerogenes and with proteus bacilli produced no renal gravel. Microscopic examination of the gravel and of the concrements revealed that the smallest formed constituents consist of roundish bodies with an onionskin-like stratification and a darker "nucleus" in the center. These smallest forms are designated as "primary bodies." Larger calculi are formed either by the joining together and fusion of such bodies or by direct concentric apposition of new layers. The colloid framework, which remains after the organic substances have been dissolved, shows the same onionskin-like stratification. In larger bodies, garland-like outlines are observable. Bacteriologic examination revealed one concrement to be free from cocci, while two others contained large numbers of cocci. A larger number of human

calculi were treated and sectioned in the same manner as were the concrements from rabbits. The phosphate calculi, nearly all of which contained cocci, showed the same microscopic pictures as did the experimental rabbit concrements. In the oxalate concrements the similarity was not so pronounced. The development of the primary bodies is supposedly due to the saturation of small drops of a colloidal or protein-like substance with urinary salts, or to the fact that the flocculation of certain colloidal substances takes place in combination with electrolytes. This would explain the atypical crystal shape and the succession of layers, of which one always has a high electrolyte and a low protein content, while the next one has the reverse composition. The author thinks that the protein substances involved in calculus formation are probably not normal but are colloids that have undergone changes and are foreign to the urine, and it appears that the staphylococci play a determining part in this process. The simultaneous modification of the urinary chemistry by these micro-organisms is the second factor in the development of the calculi. The examination of two vesical calculi, which had developed in rats under the influence of food deficient in vitamin A, revealed that they had an entirely different pathogenesis. It appears that lime débris and lime clots became deposited on cast-off epithelial cells or on groups of cells. A similar development could be observed in a rabbit following the introduction of colon bacilli. The duplication of the experiments of Rosenow and Meisser, namely, the production of renal calculi in dogs by infection of the pulp cavity, produced negative results. The attempt to produce concrements in rabbits by the continuous administration of the hormone of the parathyroids or by this hormone and the introduction of staphylococci (without ureteral stasis) resulted only in insignificant calcifications in a few of the renal tubules.

Sodium Chloride in Metabolism During Urologic Disturbances.—Strauss points out that the part played by sodium chloride in the metabolism during urologic disturbances, particularly hypertrophy of the prostate, requires especial attention, for disturbances are likely. Whereas the kidney plays the most important part in the elimination of sugar and of the substances containing nitrogen, its significance in sodium chloride elimination is secondary to that of extrarenal factors. Sodium chloride elimination has no essential significance as an indicator for the renal function, but the sodium chloride tolerance test and the determination of the elimination are important. The examination of the concentration capacity of the kidney by one or repeated tolerance tests permits conclusions about the functional capacity of the kidney. In all forms of hypertrophy of the prostate in which renal changes exist, the sodium chloride elimination is abnormal following the tolerance test. The renal impairment characteristic of hypertrophy of the prostate is a hydronephrosis due to stasis. The changes developing in case of hypertrophy of the prostate, when considered from the point of view of the elimination of sodium chloride, can be divided into three groups. Hypertension belongs to the first group, in which the elimination is normal with and without tolerance tests. To the second group, in which the elimination is abnormal during the tolerance test, belong the disorders that present the aspects of focal nephritis or of the benign and incipient stages of malignant sclerosis. The third group comprises the late forms of malignant sclerosis, in which the extrarenal factors predominate and the elimination is abnormal during and outside of the tolerance test. The extent of the renal changes and of the disturbance in the sodium chloride elimination depends on the degree and the duration of the hypertrophy of the prostate and on the intensity of the stasis. Uniform evaluation of the sodium chloride content of the serum in the course of the disease encounters considerable difficulties. Normal as well as subnormal values of the sodium chloride content of the serum are encountered in patients with hypertrophy of the prostate. Occasionally, but not always, there develops during the stage of renal insufficiency, together with the azotemia, a hyperchloremia. The sodium chloride content of the serum requires especial consideration during the period after urologic operations. Postoperative disturbances belonging to the group of hypochloremic azotemia have been observed. The reduction of the chloride values of the serum after prostatectomy or other urologic operations, together with the postoperative increase in the nonprotein nitrogen, may produce the manifest or the masked forms of this syndrome. The sodium chloride deficiency, due mostly to dietetic factors, produces a general impairment of the cells as the result of reduction of the osmotic pressure. The retention of the nitrogen containing substances in the blood represents an attempt of the kidneys to maintain the osmotic pressure. Decrease of the chloride content of the serum and increase in the rest nitrogen produce uremia-like aspects that are easily misunderstood. The prostatectomy frequently taxes the organism to such an extent that it is no longer capable of compensating for the masked metabolic disturbance. For this reason sodium chloride elimination should be given especial attention, because adequate administration of sodium chloride will counteract the metabolic disturbance.

Klinicheskaya Meditsina, Moscow

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*Abdominal Angina and Atherosclerosis of Abdominal Arteries. M. Malyatskaya.—p. 1661.
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*Effect of Malaria on Pulmonary Tuberculosis. I. I. Shirokogorov.—p. 1786.
*Good Results of Serotherapy in Botulism. I. M. Velikanov and M. Kh. Kolesnikova.—p. 1807.

Atherosclerosis of Abdominal Arteries.—According to Malyatskaya, abdominal angina has been considered by the majority of authors a clinical entity analogous in its course to angina pectoris and to intermittent claudication. Sclerosis of the abdominal aorta and of the arteries of the abdominal viscera has been considered the cause. The theories regarding the mechanism of pain production are (1) anemia of the intestinal wall resulting from narrowing of the arterial lumen by the sclerotic process, (2) alterations in the smallest arteries of the intestinal wall and in the arteries of the sympathetic abdominal ganglions, and (3) periarteritis of the sclerotic vessels and of the abdominal aorta with the extension of the inflammatory process to the neighboring sympathetic ganglions. The author studied the histories of twelve selected cases of pronounced arteriosclerotic alterations of the abdominal arteries. The celiac artery and its branches as well as the superior and inferior mesenteric arteries and their branches down to the caliber of from 2 to 3 mm. were investigated. The material was divided into two groups: six cases of pronounced sclerotic alterations of the abdominal arteries and six cases of even more advanced atherosclerosis. The symptoms in these cases did not suggest the existence of abdominal angina. In the second group the intima of the large arteries presented confluent sclerotic plaques. In one case there was almost complete thrombotic occlusion of the origin of the superior mesenteric artery and marked narrowing of the lumen of the celiac and the inferior mesenteric arteries. The author concludes that advanced sclerosis of the abdominal arteries leads to considerable narrowing of the lumen of the main arteries. This alteration, however, was not found to lead to pronounced alterations in the abdominal viscera. Alterations analogous to those found in the myocardium in cases of coronary sclerosis were not found in the intestinal wall. The author concludes that the existence of even most pronounced atherosclerosis of abdominal arteries is not sufficient alone to cause manifestations of abdominal angina.

Effect of Malaria on Pulmonary Tuberculosis.—In 800 necropsies on patients who died from acute or chronic malaria, Shirokogorov found an incidence of a primary tuberculous focus in about 25 per cent. The appearance of the focus, of the adjacent tissue and of the remote organs showed the absence of signs of secondary reactivation of the primary tuberculous infection under the influence of acute or chronic malaria. This fact was particularly noteworthy in the cases of chronic malaria complicated by grave anemia, at times of a progressive malignant type characterized by bone marrow atrophy, profound metabolic disturbances in the form of fatty or amyloid

degeneration of viscera, extreme cachexia and gangrene. The author emphasizes the absence of secondary tuberculous foci in the meninges, the intestine and the genito-urinary organs. The combination of chronic pulmonary tuberculosis with malaria is rare. In 800 necropsies of malarial patients, pulmonary tuberculosis was found in only twenty cases. The author is of the opinion that the effect of malaria on tuberculosis is not brought about by weakening of the tubercle bacillus but by the development of unknown immunobiologic factors in the course of a malarial infection. Malaria cannot be counted among the diseases that activate the tuberculous infection.

Serotherapy in Botulism. — Velikanov and Kolesnikova have treated 227 cases of botulism since 1929, 146 of which were treated with a specific serum. The serum was not given to seventy-six patients. The mortality in the first group was 18 per cent, while in the second it amounted to 93 per cent. Analysis of the first group revealed that in a number of the twenty-six fatalities the serum was administered in the agonal stage. The effectiveness of the specific serum depended on its early administration, as well as on the dose. The authors advise a dose of from 50 to 60 cc., which is to be repeated in from five to ten hours if no improvement is noted. The serum is best given intramuscularly. In two apparently hopeless cases, intraspinal introduction of 20 cc. of the serum had a remarkable effect. The authors conclude that specific serum therapy in botulism gives the best curative result.

Finska Läkaresällskapets Handlingar, Stockholm

76: 1059-1127 (Dec.) 1934

*Grave Hypophyseogenic Asthenia. J. Wahlberg.—p. 1059.
Granulocytopenia After Amidopyrine Medication. B. von Bonsdorff.—p. 1072.

Grave Hypophyseogenic Asthenia.—In Wahlberg's three cases all the symptoms of hypothyreosis except myxedema were present, the most important being marked loss of weight, lack of appetite, constipation, amenorrhea, hypothermia, bradycardia, hypotension, hypoglycemia and retarded metabolic rate. A new symptom, sclerosis of the veins, was noted. Treatment with thyroid substance gave good results. The condition is ascribed to insufficiency of the anterior lobe of the pituitary with secondary deficiency symptoms from the endocrine glands affected by the function of the pituitary body. In contrast to Simmond's hypophyseal cachexia the syndrome described depends on functional, not organic, disturbance. To stress the distinction between Simmond's disease and this disorder and to emphasize its marked pluriglandular though primarily hypophyseogenic character, the term grave hypophyseogenic asthenia is proposed.

Ugeskrift for Læger, Copenhagen

97: 35-74 (Jan. 10) 1935

*Septicemia. V. Bie and N. I. Nissen.—p. 35.
*Remarks Concerning Postanginous, Metastasizing Thrombophlebitis. R. Lund.—p. 40.
Sepsis in Puerperium in Light of Bacteriologic Examination on Necropsy: Case. L. Heerup.—p. 42.
Infectious Mononucleosis with Transition to Agranulocytosis: Case? B. Elmenhoff-Nielsen.—p. 44.
Agranulocytosis After Amidopyrine (Climaxid Tablets): Fatal Case. C. Maarssø.—p. 47.
Cosmetic Treatment in Progressive Lipodystrophy. E. Dujardin.—p. 48.
Change in Widal Reaction. C. O. Faarup and M. Kristensen.—p. 48.

Septicemia.—After emphasizing the importance of repeated chills in the prognosis of septicemia, Bie and Nissen discuss the significance of the establishment of bacteremia. Blood tests gave positive results in nineteen of forty-eight cases of septicemia. The mortality in these cases was 79 per cent; in the sixteen cases in which streptococci were found, 75 per cent; in the eight with hemolytic streptococci, 63 per cent, and in the eight with nonhemolytic streptococci, 88 per cent. In the twenty-nine cases without demonstrated bacteremia the mortality was 55 per cent. The prognostic significance of the hematologic examination, the authors state, depends mainly on the relation between the shifting to the left and the number of leukocytes, increased shifting to the left simultaneously with reduction of the leukocyte count being unfavorable. Reviewing the prognosis on the basis of the division of their cases into (1) the group in which the septicemia originated from angina, (2) the group with endocarditis and (3) the group with neither of these disorders, they find the prognosis for group 2 grave, for group 1 little better, and for group 3 relatively good. Chemotherapy has been disappointing. In tonsillogenic septicemia they would try treatment with one or two intravenous injections of polyvalent serum, and, if this proves ineffective, call in an otologist for operative intervention. Three of their more recent cases of tonsillogenic septicemia treated with polyvalent serum are described in detail. To lessen the danger of consequent shock they give acetylsalicylic acid one hour before the injection.

Postanginous, Metastasizing Thrombophlebitis. — Lund points out that the angina preceding this disease, which most often occurs between the ages of 20 and 30, is usually quite banal and is followed by an inflammatory process, generally in the peritonsillar connective tissue, possibly in the parapharyngeal tissue behind the tonsil, as a rule with abscess formation. The inflammation may not be especially marked and the abscess, usually deep seated, may not be recognized on inspection of the throat. There is tenderness in the glands at the side of the neck. Repeated chills occur and are the decisive symptoms on which diagnosis is made. Treatment is surgical, to be instituted at once, and consists in extirpation of the affected parts of the thrombosing veins. The final stage, if timely operation is not done, is metastasis to the heart and lungs.

97: 75-102 (Jan. 17) 1935

Diagnostic Significance of Myopathies in Disturbances of the Ear. G. V. T. Borries.—p. 75.
*Glycocoll Treatment in Progressive Muscular Dystrophy. C. J. Munch-Petersen.—p. 77.
Intestinal Obstruction in Child Caused by Ascarides. H. Harpøth.—p. 80.
Epidemic Myalgia on Faroe Islands. R. K. Rasmussen.—p. 83.
Poliomyelitic Ischialgia. K. Søndergaard.—p. 86.
Remarks on Treatment of Scabies. E. Tryde.—p. 87.
Attempt at Rapid and Reliable Analysis of Many Urine Tests at One Time. V. Clemmesen.—p. 87.

Glycocoll Treatment in Progressive Muscular Dystrophy.—Munch-Petersen reports that, in a case with mixed clinical picture of congenital myotonia, progressive muscular dystrophy and Little's disease, continued treatment with glycocoll was of little avail, but the treatment gave satisfactory results in a case with simultaneous development of a central paralysis and typical scapulohumeral muscular dystrophy, confirming Kostakow's experience that the best results of the treatment are attained in the purest cases. In the second instance the increased sugar reaction in the spinal fluid together with the atypical Wassermann reaction suggest a striatum disorder, presumably an epidemic encephalitis, and the possibility of a causal connection between this and the progressive muscular dystrophy is considered.

Upsala Lakareforenings Forhandlingar, Uppsala

40: 1-182 (Dec. 28) 1934

Investigations on Distribution of Sympathetic Nerves to Brachial Plexus and on Cervical Part of Ganglionated Cord in Man. M. Wrete.—p. 1.
*Periarteritis Nodosa: Two Cases. N. Gellerstedt and B. Wennerberg.—p. 95.
Decimals in Statistics. G. Dahlberg.—p. 109.
Contribution to Knowledge of Relations of Yohimbin to Vegetative Nervous System. P. Weger.—p. 113.
Solution of Formaldehyde in Treatment of Warts and Superficial Tumors of Skin, Such as Cancroids: Preliminary Report. H. Laurell.—p. 169.
Occurrence of Vitamin D in Herring. G. Blix, H. Rydin and Gösta Englund.—p. 175.

Periarteritis Nodosa.—In their first case with recent syphilitic infection in the primary sclerosis stage, the age of certain histologic changes in the blood vessels in relation to the age of the syphilitic infection and the failure, in spite of careful examination, to find spirochetes led Gellerstedt and Wennerberg to conclude that syphilis in all probability is not the primary cause of the arterial disorder. In the second instance with pronounced symptoms of polyneuritis, neurohistologic examination disclosed marked, typical changes in the intraneural blood vessel branches and, localized especially in their vicinity, degeneration in the myelin sheaths and axis cylinders, affording evidence of a causal connection between the disturbance of the nerves and the blood vessels. The secondary retrograde degeneration of the cells of the anterior horn of the spinal cord was most evident in the lumbar region.